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<b>(21) International Application Number: PCT/EP99/05991</b> <b>(22) International Filing Date: 16 August 1999 (16.08.99)</b>  <b>(30) Priority Data:</b> 9817796.7           14 August 1998 (14.08.98)   GB 98310694.9       23 December 1998 (23.12.98)   EP  <b>(71) Applicant (for all designated States except US): JANSSEN PHARMACEUTICA N.V. [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE).</b>  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only): CONTRERAS, Roland, Henri [BE/BE]; University of Gent, K.L. Ledeganckstraat 35, B-9000 Gent (BE). NELISSEN, Bart [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). DE BACKER, Marianne, Denise [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). LUYTEN, Walter, Herman, Maria, Louis [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). VIAENE, Jasmine, Elza [BE/BE]; University of Gent, K.L. Ledeganckstraat 35, B-9000 Gent (BE). LOGGHE, Marc, George [BE/BE]; University of Gent, K.L. Ledeganckstraat 35, B-9000 Gent (BE).</b>	<b>(74) Agent: BOULT WADE TENNANT; 27 Fumival Street, London EC4A 1PQ (GB).</b>  <b>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</b>  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>	
<b>(54) Title: DRUG TARGETS IN CANDIDA ALBICANS</b>		
<b>(57) Abstract</b> <p>The present invention is concerned with a method of identifying compounds which selectively modulate expression of polypeptides which are crucial for growth and survival of <i>Candida albicans</i>, which method comprises: (a) contacting a compound to be tested with one or more <i>Candida albicans</i> cells having a mutation in a nucleic acid molecule corresponding to the sequences according to any of claims 1 to 8 which mutation results in overexpression or underexpression of said polypeptides, in addition to contacting one or more wild type <i>Candida albicans</i> cells with said compound, (b) monitoring the growth and/or activity of said mutated cell compared to said wild type; wherein differential growth or activity of said one or more mutated <i>Candida</i> cells is indicative of selective action of said compound on a polypeptide or another polypeptide in the same or a parallel pathway. Also disclosed in the present invention are compounds identified and the sequences themselves which are critical for survival and growth of <i>Candida albicans</i>.</p>		

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## DRUG TARGETS IN CANDIDA ALBICANS

The present invention is concerned with the identification of genes or functional fragments thereof from *Candida albicans* which are critical for growth and cell division and which genes may be used as selective drug targets to treat *Candida albicans* associated infections. Novel nucleic acid sequences from *Candida albicans* are also provided and which encode the polypeptides which are critical for growth of *Candida albicans*.

Opportunistic infections in immunocompromised hosts represent an increasingly common cause of mortality and morbidity. *Candida* species are among the most commonly identified fungal pathogens associated with such opportunistic infections, with *Candida albicans* being the most common species. Such fungal infections are thus problematical in, for example, AIDS populations in addition to normal healthy women where *Candida albicans* yeasts represent the most common cause of vulvovaginitis.

Although compounds do exist for treating such disorders, such as for example, amphotericin, these drugs are generally limited in their treatment because of their toxicity and side effects. Therefore, there exists a need for new compounds which may be used to treat *Candida* associated infections in addition to compounds which are selective in their action against *Candida albicans*.

Classical approaches for identifying anti-fungal compounds have relied almost exclusively on inhibition of fungal or yeast growth as an endpoint. Libraries of natural products, semi-synthetic, or synthetic chemicals are screened for their ability to kill or arrest growth of the target pathogen or a related nonpathogenic model organism. These tests are

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cumbersome and provide no information about a compounds mechanism of action. The promising lead compounds that emerge from such screens must then be tested for possible host-toxicity and detailed  
5 mechanism of action studies must subsequently be conducted to identify the affected molecular target.

The present inventors have now identified a range of nucleic acid sequences from *Candida albicans* which encode polypeptides which are critical for its  
10 survival and growth. These sequences represent novel targets which can be incorporated into an assay to selectively identify compounds capable of inhibiting expression of such polypeptides and their potential use in alleviating diseases or conditions associates  
15 with *Candida albicans* infection.

Therefore, according to a first aspect of the invention there is provided a nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which  
20 nucleic acid molecule comprises any of the sequences of nucleotides in Sequence ID Numbers 1, 2, 3, 5, 10, 11, 12, 14, 16, 18, 20, 21, 23, 25, 27, 29, 31, 33, 37, 39, 41, 44, 45, 46, 49, 50, 52, 55, 57, 59, 61, 63, 65, 67, 70, 72, 74, 76, 78, 80, 81, 83, 85, 87,  
25 89, 91, 93, 95, 97, 99, 101, 104, 106, 108, 110 and 113, or the sequences of nucleotides identified in Figures 9 to 13.

Whilst the molecules defined herein have been established as being critical for growth and  
30 metabolism of *Candida albicans*, for some of the molecules no apparent functionality has been assigned by virtue of the fact that no functionally related sequences in other prokaryotic or eukaryotic organism can be found in respective databases. Thus,  
35 advantageously these sequences may be species specific in which case they may be used as selective targets for treatment of diseases mediated by *Candida*



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Albicans infection. Thus, in one aspect of the invention the nucleic acid molecules preferably comprise the sequences identified in sequence ID Nos 1, 2, 3, 5, 10, 11, 12, 14, 16, 17, 18, 46, 49, 50, 52, 55, 57, 59, 61, 63, 65, 87, 89, 91, 93, 95, 97, 99, 101, 104, 106, 108, and 110 and the corresponding polypeptide sequences identified in Table 1.

Some of sequences according to invention have been assigned a particular function. Nucleic acid molecules according to this aspect of the invention comprise any of the sequences as described in sequence ID Nos, 20, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 45, 65, 70, 72, 74, 76, 78, 80, 81, 83, 85 and 113 and the corresponding polypeptides identified in Table 1

Letters utilised in the nucleic acid sequences according to the invention to represent the genetic code and which are not recognisable as letters of the genetic code signify a position in the nucleic acid sequence where one or more of bases A, G, C or T can occupy the nucleotide position. Representative ambiguity codes used to identify the range of bases which can be used are as follows:

25	M:	A or C
	R:	A or G
	W:	A or T
	S:	C or G
	Y:	C or T
30	K:	G or T
	V:	A or C or G
	H:	A or C or T
	D:	A or G or T
	B:	C or G or T
35	N:	G or A or T or C

In one embodiment of the above identified aspects

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of the invention the nucleic acid may comprise a mRNA molecule or alternatively a DNA and preferably a cDNA molecule.

Also provided by the present invention is a  
5 nucleic acid molecule capable of hybridising to the nucleic acid molecules according to the invention under high stringency conditions, such as for example, an antisense molecule.

Stringency of hybridisation as used herein refers  
10 to conditions under which polynucleic acids are stable. The stability of hybrids is reflected in the melting temperature ( $T_m$ ) of the hybrids.  $T_m$  can be approximated by the formula:

15 
$$81.5^{\circ}\text{C} + 16.6 (\log_{10}[\text{Na}^+] + 0.41 (\% \text{G\&C}) - 6001/1$$

wherein 1 is the length of the hybrids in nucleotides.  $T_m$  decreases approximately by 1-1.5°C with every 1% decrease in sequence homology.

20 The nucleic acid capable of hybridising to nucleic acid molecules according to the invention will generally be at least 70%, preferably at least 80 or 90% and more preferably at least 95 to 97% homologous to the nucleotide sequences according to the  
25 invention.

The DNA molecules according to the invention may, advantageously, be included in a suitable expression vector to express polypeptides encoded therefrom in a suitable host.

30 The present invention also comprises within its scope proteins or polypeptides encoded by the nucleic acid molecules according to the invention or a functional equivalent, derivative or bioprecursor thereof.

35 Therefore, according to a further aspect of the invention there is provided a polypeptide which is critical for the growth and survival of Candida

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albicans comprising an amino acid sequence of any of Sequence ID Numbers 4, 6 to 9, 13, 15, 19, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 43, 47, 48, 51, 53, 54, 56, 58, 60, 62, 64, 66, 68, 69, 71, 73, 75, 77, 79, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 103, 105, 107, 109, 111, 112, 114 or the sequences illustrated in Figures 14 or 15.

An expression vector according to the invention includes a vector having a nucleic acid according to the invention operably linked to regulatory sequences, such as promoter regions, that are capable of effecting expression of said DNA fragments. The term "operably linked" refers to a juxta position wherein the components described are in a relationship permitting them to function in their intended manner. Such vectors may be transformed into a suitable host cell to provide for expression of a polypeptide according to the invention. Thus, in a further aspect, the invention provides a process for preparing polypeptides according to the invention which comprises cultivating a host cell, transformed or transfected with an expression vector as described above under conditions to provide for expression by the vector of a coding sequence encoding the polypeptides, and recovering the expressed polypeptides.

The vectors may be, for example, plasmid, virus or phage vectors provided with an origin of replication, optionally a promoter for the expression of said nucleotide and optionally a regulator of the promoter. The vectors may contain one or more selectable markers, such as, for example, ampicillin resistance.

Polynucleotides according to the invention may be inserted into the vectors described in an antisense orientation in order to provide for the production of antisense RNA. Antisense RNA or other antisense

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nucleic acids may be produced by synthetic means.

In accordance with the present invention, a defined nucleic acid includes not only the identical nucleic acid but also any minor base variations including in particular, substitutions in bases which result in a synonymous codon (a different codon specifying the same amino acid residue) due to the degenerate code in conservative amino acid substitutions. The term "nucleic acid sequence" also includes the complementary sequence to any single stranded sequence given regarding base variations.

The present invention also advantageously provides nucleic acid sequences of at least approximately 10 contiguous nucleotides of a nucleic acid according to the invention and preferably from 10 to 50 nucleotides. These sequences may, advantageously be used as probes or primers to initiate replication, or the like. Such nucleic acid sequences may be produced according to techniques well known in the art, such as by recombinant or synthetic means. They may also be used in diagnostic kits or the like for detecting the presence of a nucleic acid according to the invention. These tests generally comprise contacting the probe with the sample under hybridising conditions and detecting for the presence of any duplex or triplex formation between the probe and any nucleic acid in the sample.

According to the present invention these probes may be anchored to a solid support. Preferably, they are present on an array so that multiple probes can simultaneously hybridize to a single biological sample. The probes can be spotted onto the array or synthesised *in situ* on the array. (See Lockhart et al., Nature Biotechnology, vol. 14, December 1996 "Expression monitoring by hybridisation to high density oligonucleotide arrays". A single array can contain more than 100, 500 or even 1,000 different

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probes in discrete locations.

Advantageously, the nucleic acid sequences, according to the invention may be produced using such recombinant or synthetic means, such as for example, using PCR cloning mechanisms which generally involve making a pair of primers, which may be from approximately 10 to 50 nucleotides to a region of the gene which is desired to be cloned, bringing the primers into contact with mRNA, cDNA, or genomic DNA from a human cell, performing a polymerase chain reaction under conditions which bring about amplification of the desired region, isolating the amplified region or fragment and recovering the amplified DNA. Generally, such techniques as defined herein are well known in the art, such as described in Sambrook et al (Molecular Cloning: a Laboratory Manual, 1989).

The nucleic acids or oligonucleotides according to the invention may carry a revealing label. Suitable labels include radioisotopes such as  $^{32}\text{P}$  or  $^{35}\text{S}$ , enzyme labels or other protein labels such as biotin or fluorescent markers. such labels may be added to the nucleic acids or oligonucleotides of the invention and may be detected using known techniques *per se*.

The polypeptide or protein according to the invention includes all possible amino acid variants encoded by the nucleic acid molecule according to the invention including a polypeptide encoded by said molecule and having conservative amino acid changes. Polypeptides according to the invention further include variants of such sequences, including naturally occurring allelic variants which are substantially homologous to said polypeptides. In this context, substantial homology is regarded as a sequence which has at least 70%, preferably 80 or 90% amino acid homology with the polypeptides encoded by

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the nucleic acid molecules according to the invention.

A nucleic acid which is particularly advantageous is one comprising the sequences of nucleotides according to Seq ID Nos 1 and 91 in which are specific to *Candida albicans* with no functionally related sequences in other prokaryotic or eukaryotic organism as yet identified from the respective genomic databases.

Nucleotide sequences according to the invention are particularly advantageous for selective therapeutic targets for treating *Candida albicans* associated infections. For example, an antisense nucleic acid capable of binding to the nucleic acid sequences according to the invention may be used to selectively inhibit expression of the corresponding polypeptides, leading to impaired growth of the *Candida albicans* with reductions of associated illnesses or diseases.

The nucleic acid molecule or the polypeptide according to the invention may be used as a medicament, or in the preparation of a medicament, for treating diseases or conditions associated with *Candida albicans* infection.

Advantageously, the nucleic acid molecule or the polypeptide according to the invention may be provided in a pharmaceutical composition together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

Antibodies to the protein or polypeptide of the present invention may, advantageously, be prepared by techniques which are known in the art. For example, polyclonal antibodies may be prepared by inoculating a host animal, such as a mouse, with the polypeptide according to the invention or an epitope thereof and recovering immune serum. Monoclonal antibodies may be prepared according to known techniques such as described by Kohler R. and Milstein C., Nature

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(1975) 256, 495-497.

Antibodies according to the invention may also be used in a method of detecting for the presence of a polypeptide according to the invention, which method  
5 comprises reacting the antibody with a sample and identifying any protein bound to said antibody. A kit may also be provided for performing said method which comprises an antibody according to the invention and means for reacting the antibody with said sample.

10 Proteins which interact with the polypeptide of the invention may be identified by investigating protein-protein interactions using the two-hybrid vector system first proposed by Chien et al (1991).

This technique is based on functional  
15 reconstitution *in vivo* of a transcription factor which activates a reporter gene. More particularly the technique comprises providing an appropriate host cell with a DNA construct comprising a reporter gene under the control of a promoter regulated by a transcription  
20 factor having a DNA binding domain and an activating domain, expressing in the host cell a first hybrid DNA sequence encoding a first fusion of a fragment or all of a nucleic acid sequence according to the invention and either said DNA binding domain or said activating  
25 domain of the transcription factor, expressing in the host at least one second hybrid DNA sequence, such as a library or the like, encoding putative binding proteins to be investigated together with the DNA binding or activating domain of the transcription  
30 factor which is not incorporated in the first fusion; detecting any binding of the proteins to be investigated with a protein according to the invention by detecting for the presence of any reporter gene product in the host cell; optionally isolating second  
35 hybrid DNA sequences encoding the binding protein.

An example of such a technique utilises the GAL4

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protein in yeast. GAL4 is a transcriptional activator of galactose metabolism in yeast and has a separate domain for binding to activators upstream of the galactose metabolising genes as well as a protein binding domain. Nucleotide vectors may be constructed, one of which comprises the nucleotide residues encoding the DNA binding domain of GAL4. These binding domain residues may be fused to a known protein encoding sequence, such as for example the nucleic acids according to the invention. The other vector comprises the residues encoding the protein binding domain of GAL4. These residues are fused to residues encoding a test protein. Any interaction between polypeptides encoded by the nucleic acid according to the invention and the protein to be tested leads to transcriptional activation of a reporter molecule in a GAL-4 transcription deficient yeast cell into which the vectors have been transformed. Preferably, a reporter molecule such as  $\beta$ -galactosidase is activated upon restoration of transcription of the yeast galactose metabolism genes.

Further provided by the present invention is one or more *Candida albicans* cells comprising an induced mutation in the DNA sequence encoding the polypeptide according to the invention.

A further aspect of the invention provides a method of identifying compounds which selectively inhibit or interfere with the expression, or the functionality of polypeptides expressed from the nucleotides sequences according to the invention or the metabolic pathways in which these polypeptides are involved and which are critical for growth and survival of *Candida albicans*, which method comprises (a) contacting a compound to be tested with one or more *Candida albicans* cells having a mutation in a nucleic acid molecule according to the invention which mutation results in overexpression or underexpression



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of said polypeptides in addition to one or more wild type *Candida* cells, (b) monitoring the growth and/or activity of said mutated cell compared to said wild type wherein differential growth or activity of said one or more mutated *Candida* cells provides an indication of selective action of said compound on said polypeptide or another polypeptide in the same or a parallel pathway.

Compounds identifiable or identified using the method according to the invention, may advantageously be used as a medicament, or in the preparation of a medicament to treat diseases or conditions associated with *Candida albicans* infection. These compounds may also advantageously be included in a pharmaceutical composition together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

A further aspect of the invention provides a method of identifying DNA sequences from a cell or organism which DNA encodes polypeptides which are critical for growth or survival, which method comprises (a) preparing a cDNA or genomic library from said cell or organism in a suitable expression vector which vector is such that it can either integrate into the genome in said cell or that it permits transcription of antisense RNA from the nucleotide sequences in said cDNA or genomic library, (b) selecting transformants exhibiting impaired growth and determining the nucleotide sequence of the cDNA or genomic sequence from the library included in the vector from said transformant. Preferably, the cell or organism may be any yeast or filamentous fungi, such as for example, *Saccharomyces cerevisiae*, *Saccharomyces pombe* or *Candida albicans*.

A further aspect of the invention provides a pharmaceutical composition comprising a compound according to the invention together with a

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pharmaceutically acceptable carrier, diluent or excipient therefor.

The present invention may be more clearly understood with reference to the accompanying example,  
5 which is purely exemplary, with reference to the accompanying drawings wherein:

Figure 1:

is an illustration of A)  
Intergration of the antisense  
10 library plasmid (here shown as a linear fragment) at a site (eg. *GAL1* promoter region) within the genome which is non-homologous to the insert DNA. As a result the *GAL1p* region is duplicated and antisense RNA can be formed from  
15 GENE X upon induction of *GAL1p*, and B) Intergration due to homologous recombination of the  
20 gene insert (GENE X) of an antisense library clone (here shown as a linear fragment) with the homologous gene (gene x) within the *Candida* genome. As a result this gene is duplicated. The first copy of the gene gene X,  
25 is flanked by upstream its endogenous promoter and downstream, oppositely-oriented, the *GAL1* promoter resulting in a so-called "collision construct". Antisense RNA can be formed from  
30 GENE X upon induction of *GAL1p*. The second copy of the gene, Gene X, is devoid of a promoter and  
35 will not be transcribed.

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Figure 2: is an illustration of the vectors used for the preparation of a cDNA antisense library, pGAL1PNiST-1, (left) and a genomic library, pGAL1PNiST-1 (right).

Figure 3: Growth curves in S-glucose and S-galactose medium of respectively the wild type CAI-4 strain and two transformants (clone 36 and 38) showing antisense induced reduction in growth and overall impaired growth, respectively. Growth curves in S-glucose+maltose and S-galactose+maltose medium of respectively the wild type CAI-4 strain and transformants resulting from antisense library transformation.

Figure 4: is an illustration of promoter activity of the *C. albicans* GAL1 promoter in the absence and presence of maltose as a carbon source.

Figures 5: is a Northern blot analysis of *C. albicans* mRNA in wild type and clone 36 using a SAM2 and a TEF3 specific probe.

Figures 6: is A) a Northern blot analysis of sequences of *C. albicans* mRNA in wild type and clone 38 using a RNR1 and an ACT1 specific probe; and B) Real Time Quantitative PCR

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on *C. albicans* mRNA in wild type and clone 38 using a *RNR1* and *ACT1* specific fluorogenic probe.

5

Figure 7: is a nucleotide sequence of plasmid pGAL1PNiST-1.

10

Figure 8: is a nucleotide sequence of plasmid pGAL1PSiST-1.

15

Figure 9: is a nucleotide sequence of clone 38 which has been assigned *RNR1* functionally.

Figure 10: is a nucleotide sequence of clone 113g4.

20

Figure 11: is a nucleotide sequence of clone 207g4

Figure 12: is a nucleotide sequence of clone 66g4.

25

Figure 13: is a nucleotide sequence of clone 36 which has been assigned Sam2 functionally.

30

Figure 14: is an amino acid sequence of clone 38.

Figure 15: is an amino acid sequence of clone 36.

35

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Figures 16 to 70 are growth curves of *Candida albicans* showing antisense induced reduction in growth by inhibition of molecules according to the invention.

### Example

Identification of novel drug targets in *C. albicans* by anti-sense and disruptive integration

The principle of the approach is based on the fact that when a particular *C. albicans* mRNA is inhibited by producing the complementary anti-sense RNA, the corresponding protein will decrease. If this protein is critical for growth or survival, the cell producing the anti-sense RNA will grow more slowly or will die.

Since anti-sense inhibition occurs at mRNA level, the gene copy number is irrelevant, thus allowing applications of the strategy even in diploid organisms.

Anti-sense RNA is endogenously produced from an integrative or episomal plasmid with an inducible promoter; induction of the promoter leads to the production of a RNA encoded by the insert of the plasmid. This insert will differ from one plasmid to another in the library. The inserts will be derived from genomic DNA fragments or from cDNA to cover to the extent possible- the entire genome.

The vector is a proprietary vector allowing integration by homologous recombination at either the homologous insert or promoter sequence in the *Candida* genome. After introducing plasmids from cDNA or genomic libraries into *C. albicans*, transformants are screened for impaired growth after promoter (& thus anti-sense) induction in the presence of lithium acetate. Lithium acetate prolongs the G1 phase and

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thus allows anti-sense to act during a prolonged period of time during the cell cycle. Transformants which show impaired growth in both induced and non-induced media, thus showing a growth defect due to integrative disruption, are selected as well.

Transformants showing impaired growth are supposed to contain plasmids which product anti-sense RNA or mRNAs critical for growth or survival. Growth is monitored by measuring growth-curves over a period of time in a device (Bioscreen Analyzer, Labsystems) which allows simultaneous measurement of growth-curves of 200 transformants.

Subsequently plasmids can be recovered from the transformants and the sequence of their inserts determined, thus revealing which mRNA they inhibit. In order to be able to recover the genomic or cDNA insert which has integrated into the Candida genome, genomic DNA is isolated, cut with an enzyme which cuts only once into the library vector (and estimated approx. every 4096 bp in the genome) and relegated. PCR with primers flanking in the insert will yield (Partial) genomic or cDNA inserts as PCR fragments which can directly be sequenced. This PCR analysis (on ligation reaction) will also show us how many integrations occurred. Alternatively the ligation reaction is transformed to E. coli and PCR analysis is performed on colonies or on plasmid DNA derived thereof.

This method is employed for a genome wide search for novel C. albicans genes which are important for growth or survival.

#### MATERIALS AND METHODS

##### Constructi n of pGallNIST-1

pGAL1PNiST-1 (integrative antisense SfiI-NotI vector)

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was constructed as described by Logghe et al.,  
submitted.

#### Construction of pGAL1PSiST-1

5 The vector pGAL1PSiST-1 (integrative SfiI-SfiI vector)  
was created for cloning the small genomic DNA  
fragments behind the GAL1 promoter. The only  
10 difference with pGAL1PNiST-1 is that the hIFNb insert  
fragment in pGAL1PSiST-1 is flanked by two SfiI sites  
instead of a SfiI and a NotI site as in pGAL1PNiST-1.  
To construct pGAL1PSiST-1 the EcoRI-HindIII fragment,  
containing hIFNb flanked by a SfiI and a NotI site, of  
pMAL2pHiET-3 (Logghe M., unpublished) was exchanged by  
15 the EcoRI-HindIII fragment, containing hIFNb flanked  
by two SfiI sites, from YCp50S-S (an E. coli / S.  
cerevisiae shuttle vector derived from the plasmid  
YCp50, which is deposited in the ATCC collection  
(number 37419; Thrash et al., 1985); an EcoRI-HindIII  
20 fragment, containing the gene hIFNb, which is flanked  
by two SfiI sites, was inserted in YCp50, creating  
YCp50S-S), resulting into plasmid pMAL2PSiST-1. The  
MAL2 promoter from pMAL2PSiST-1 (by a NaeI-FspI  
digest) was further replaced by the GAL1 promoter from  
25 pGAL1PNiST-1 (via a XhoI-SalI digest), creating the  
vector pGAL1PSiST-1.

#### Preparation of C. albicans genomic library

30 A C. albicans genomic DNA library with small DNA  
fragments was prepared for integrative disruption.  
Genomic DNA of C. albicans B2630 (ATCC No. 44858) was  
isolated following a modified protocol of Blin and  
Stafford (1976). To obtain enrichment for genomic DNA  
35 fragments of the desired size, the genomic DNA was  
partially digested. Enrichment of small DNA fragments

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was obtained with 70 units of AluI on 10 mg of genomic DNA for 20 min. T4 DNA polymerase (Boehringer) and dNTPs (Boehringer) were added to polish the DNA ends. After extraction with phenol-chloroform the digest was size-fractionated on an agarose gel. The genomic DNA fragments with a length of 0.5 to 1.25 kb were eluted from the gel by centrifugal filtration (Zhu et al., 1985). SfiI adaptors (5' GTTGGCCTTTT) were attached to the DNA ends (blunt) to facilitate cloning of the fragments into the vector. After ligation of these adaptors to the DNA fragments a second size-fractionation was performed on an agarose gel. The small genomic DNA fragments were cloned upstream of the GAL1 promoter in the vector pGAL1PSiST-1. Qiagen-purified pGAL1PSiST-1 plasmid DNA was digested with SfiI and the largest vector fragment eluted from the gel by centrifugal filtration (Zhu et al., 1985). The ligation mix was electroporated to MC1061 (...) E. coli cells.

20

#### C. albicans cDNA library

Total RNA was extracted from C. albicans strain B2630 grown on respectively minimal (SD) and rich (YPD) medium as described by Sambrook et al. (1989). mRNA was prepared from total RNA using the Invitrogen Fast Track procedure. First strand cDNA was synthesised with Superscript Reverse Transcriptase (BRL) and with an oligo dT-NotI Primer adapter. After second strand synthesis, cDNA was polished with Klenow enzyme and purified over a Sephacryl S-400 spin column. Phosphorylated SfiI adapters were then ligated to the cDNA, followed by digestion with the NotI restriction enzyme. The SfiI/NotI cDNA was purified and sized on a Biogel column A150M. cDNA was ligated in a NotI/SfiI opened pGAL1PNiST-1 vector.

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**Transformation of *C. albicans***

*C. albicans* CAI-4 (URA3::imm434/URA3::imm434) was kindly provided by Dr. William Fonzi, Georgetown University (Fonzi and Irwin, 1993). CAI-4 was transformed with above described cDNA library or genomic library using a modified spheroplast method (Logghe M., submitted). Cells were plated on minimal medium supplemented with glucose and sorbitol (SD (0.67% Yeast Nitrogen base w/o amino acids + 2% glucose), 1 M sorbitol) plates using 0.4 cm glass-pearls (Glaverbel, Belgium) and incubated for 2-3 days at 30°C.

**Screening for mutants**

Starter cultures were set up by inoculating each colony in 1 ml SD medium and incubating overnight at 30°C and 300 rpm. Cell densities were determined using a Coulter counter (Coulter Z1; Coulter electronics limited). 250.000 cells/ml were inoculated in SD medium for a total volume of 1ml and cultures were incubated for 24 hours at 30°C and 300 rpm. Cultures were washed in minimal medium without glucose (S) and the pellet resuspended in 650 ml S medium. 8 µl of this culture was used for inoculating 400 µl cultures in a Honeywell-100 plate (Bioscreen analyzer, Labsystems). Each transformant was grown for three days in S medium containing 50 mM LiAc; pH 6.0, with 2% glucose +/- 2% maltose or 2% galactose +/- 2% maltose respectively while shaking (high intensity) every 3 minutes for 20 seconds. Optical densities were measured every hour and growth curves were generated automatically (Bioscreen analyzer; Labsystems).

**Construction of LAC4/ pGAL1PN1ST-1**

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pGAL1PNiST-1 vector was cut with StuI in order to release the stuffer fragment and subsequently dephosphorylated (CIP, Boehringer). Plasmid pRS1004, obtained from J. Ernst (University of Duesseldorf, Germany), was cut with PvuII/XbaI in order to release the K. lactis  $\beta$ -galactosidase (EC 3.2.1.23; LAC4) reporter gene and Klenow-treated. The LAC4 PvuII/XbaI blunted reporter gene fragment from pRS1004 was ligated into StuI opened pGAL1PNiST-1 resulting in the integrative plasmid LAC4/pGAL1PNiST-1

#### Measurement of GAL1 promoter activity

C. albicans strain CAI-4 was transformed with LAC4/pGAL1PNiST-1 using the modified spheroplast method (Logghe et al., submitted). Resulting transformants were grown in 5 ml of respectively non-induction (SD +/- maltose) and induction (S+ galactose +/- maltose) medium and further processed as described by Leuker et al. (1997).

#### Isolation of genomic or cDNA inserts

Potentially interesting transformants were grown in 1.5 ml SD overnight. Genomic DNA was isolated using the Nucleon MI Yeast kit (Amersham) and the concentration of genomic DNA was estimated by analyzing a sample on a 0.7% agarose gel in 0.5x TBE and comparison to a known standard molecular weight marker. 20 ng of genomic DNA was digested for three hours with an enzyme that cuts uniquely in the library vector (SacI for the genomic library; PstI for the cDNA library), treated with RNase A (Boehringer) and incubated for 20 minutes at 65°C to inactivate the enzyme. Samples were phenol/chloroform extracted twice and precipitated using NaOAc/ethanol. The resulting

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pellet was resuspended in 500  $\mu$ l ligation mixture (1 x ligation buffer and T4 DNA ligase; both from Boehringer) and incubated overnight at 16°C.

5 After denaturation (10 min 65°C), purification (phenol/chloroform extraction) and precipitation (NaOAc/ethanol) the pellet was resuspended in 10  $\mu$ l MilliQ (Millipore) water.

Inverse PCR was performed on 1  $\mu$ l of the precipitated ligation reaction using library vector specific  
10 primers (Figure 1) (3pGALSistPCR: 5' GAG-GGC-GTG-AAT-GTA-AGC-GTG 3' and 5pGALNistPCR: 5'GAG-TTA-TAC-CCT-GCA-GCT-CGA-C 3' for the genomic library;  
3pGALNistPCR: 5' TGA-GCA-GCT-CGC-CGT-CGC-GC 3' and 5pGALNistPCR for the cDNA library; all primers from  
15 Eurogentec) for 30 cycles each consisting of (a) 1 min at 95 °C, (b) 1 min at 61 (or 57 °C for the cDNA library primers), and (c) 3 min at 72 °C. In the reaction mixture 2.5 units of Taq polymerase (Boehringer) with TaqStart antibody (Clontech) (1:1)  
20 were used, and the final concentrations were 0.2  $\mu$ M of each primer, 3 mM MgCl<sub>2</sub> (Perkin Elmer Cetus) and 200  $\mu$ M dNTPs (Perkin Elmer Cetus). All PCR reactions were performed in a Robocycler (Stratagene).

PCR analysis is also performed on genomic DNA isolated  
25 from the transformants using primers 3pGALSistPCR and 5pGALNistPCR for the genomic library transformants and using primers oligo23': 5' TGC-AGC-TCG-ACC-TCG-AGG 3' and oligo25: 5' GCG-TGA-ATG-TAA-GCG-TGA-C 3' ( $T_{hybr}$  = 53 °C) for the cDNA library transformants.

30 Resulting PCR products were purified using the PCR purification kit (Qiagen) and were quantified by comparison of band intensity with the intensity of DNA marker bands on a ethidium bromide stained agarose gel.

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Sequence determination

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The amount of PCR product (expressed in ng) put in the sequencing reaction is calculated as the length of the PCR product in basepairs divided by 10. DNA sequencing reactions were performed using the ABI Prism BigDye Terminator Cycle Sequencing Ready Reaction Kit according to the instructions of the manufacturer (PE Applied Biosystems, Foster City, CA) except for the following modifications. The total reaction volume was reduced to 15  $\mu$ l. Reaction volumes of individual reagents were changed accordingly. The 6.0  $\mu$ l Terminator Ready Reaction Mix was replaced by a mixture of 3.0  $\mu$ l Terminator Ready Reaction Mix + 3.0  $\mu$ l Half Term (GENPAK Limited, Brighton, UK). After cycle sequencing, reaction mixtures were purified over Sephadex G50 columns prepared on Multiscreen HV opaque Microtiter plates (Millipore, Molsheim, Fr) and were dried in a speedVac. Reaction products were resuspended in 3  $\mu$ l loading buffer. Following denaturation for 2 min at 95°C, 1  $\mu$ l of sample was applied on a 5% Long Ranger Gel (36 cm well-to-read) prepared from Singel Packs according to the supplier's instructions (FMC BioProducts, Rockland, ME). Samples were run for 7 hours 2X run on a ABI 377XL DNA sequencer. Data collection version 2.0 and Sequence analysis version 3.0 (for basecalling) software packages are from PE Applied Biosystems.

#### Sequence analysis

Nucleotide sequences were imported in the VectorNTI software package (InforMax Inc, North Bethesda, MD, USA), and the vector and insert regions of the sequences were identified. Sequence similarity searches against public and commercial sequence databases were performed with the BLAST software package (Altschul et al., 1990) version 1.4. Both the original nucleotide sequence and the six-frame conceptual translations of the insert region were used

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as query sequences. The used public databases were the EMBL nucleotide sequence database (Stoesser et al., 1998), the SWISS-PROT protein sequence database and its supplement TrEMBL (Bairoch and Apweiler, 1998),  
5 and the ALCES Candida albicans sequence database (Stanford University, University of Minnesota). The commercial sequence databases used were the LifeSeq<sup>®</sup> human and PathoSeq<sup>™</sup> microbial genomic databases (Incyte Pharmaceuticals Inc., Palo Alto, CA, USA), and  
10 the GENESEQ patent sequence database (Derwent, London, UK). Three major results were obtained on the basis of the sequence similarity searches: function, novelty, and specificity. A putative function was deduced on the basis of the similarity with sequences with a  
15 known function, the novelty was based on the absence or presence of the sequences in public databases, and the specificity was based on the similarity with vertebrate homologues.

The 5' UTR region of the SAM2 gene was analysed using  
20 the "Findpatterns" algorithm of the Genetics Computer Group (GCG) software package (University of Wisconsin, USA).

#### Northern blot analysis

25 Cells were grown to OD<sub>600</sub> ~ 1.0 and total RNA was prepared using the RNeasy midi kit (Qiagen) according to the manufacturer's instructions. RNA concentrations were determined spectrophotometrically by measuring optical densities at 260 nm in a UV-1601 UV-visible  
30 spectrophotometer (Shimadzu) and 5 µg of each sample was resolved onto a 1% formaldehyde gel and run in 1 x formaldehyde gel running buffer (5prime-3prime) at 3.5 V/cm. RNA was stained for 20 minutes using SYBR Green II stain (Molecular probes) 1/10000 diluted in 1x  
35 formaldehyde gel running buffer (5prime-3prime) and subsequently transferred to Hybond-N+ nylon membrane (Amersham) by overnight capillary blotting in 20 x

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SSC. DIG-labeled probes were prepared using DIG-dUTP (Boehringer Mannheim) at a 1:3 or 1:6 dTTP:DIG-dUTP ratio, 10 pg of template plasmid DNA, 1x PCR buffer II (Perkin Elmer Cetus), 10  $\mu$ M of each primer (Eurogentec), 0.2 mM of dATP, dCTP and dGTP (Perkin Elmer Cetus), 2.5 mM MgCl<sub>2</sub> (Perkin Elmer Cetus), 5% DMSO and 1.25 units Taq polymerase (Boehringer). The membrane was prehybridized at 50°C (DNA probes) or at 68°C (RNA probes) in DIG Easy Hyb (Boehringer Mannheim) for minimum 1 hour. Hybridization was performed using 1  $\mu$ l PCR reaction product (= 1/50 of the total volume)/ml DIG Easy Hyb. The probes were denatured by heating the PCR reaction for 10 minutes at 96°C, then quick-chilling on ice. The probe was kept on ice for 5 minutes, centrifuged briefly and diluted in pre-warmed DIG Easy Hyb solution. The entire probe solution was filtered through a 0.45  $\mu$ m filter (Millex HV, Millipore) prior to use. Hybridizations were carried out overnight. Post-hybridization, membranes were washed twice 15 minutes with 2x SSC/0.1% SDS at room temperature and twice 15 minutes with 0.1x SSC/0.1% SDS at 68°C. Detection was performed using the DIG Wash and Block Buffer Set as described by the manufacturer (Boehringer Mannheim Mannheim) and the blot was exposed to Kodak XAR-5 film for 1 hour at ambient temperature.

Real time quantitation of mRNA transcript PCR quantitations using specific primers and probes were performed according to the TaqMan procedure (Livak et al., 1995; Orlando et al., 1998) using the ABI Prism 7700 sequence detector (Applied Biosystems). Primers and probes for ACT1 (b-actin) and RNR1 genes were designed using the PrimerExpress software system (Perkin Elmer Cetus).

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Cells were grown to OD<sub>600</sub> ~ 1.0 and total RNA was prepared using the RNeasy midi kit (Qiagen) according to the manufacturer's instructions. All RNA samples were DNaseI (Boehringer-Mannheim, RNase-free)-treated at 20 U/μg in 50 μl solution for 40 min at ambient temperature, phenol/chloroform-extracted and precipitated. Pellets were dissolved in 20 ml MilliQ water (Millipore) and RNA concentrations were determined spectrophotometrically. First-strand cDNA synthesis was performed in a final volume of 20 μl containing 1x Superscript RT buffer (Life Technologies), 10 mM DTT, 125 μM of each dNTP, 50 μM hexamer primers (Life Technologies) and 1 mg RNA. Mixtures were incubated for 10 min. at ambient temperature and 1 μl was removed and diluted 1:4 for the non-amplification control (NAC); 20 U Superscript reverse transcriptase (Life Technologies) was added and the reaction was incubated for 1 hour at 42 °C. The enzyme was inactivated for 10 min at 70°C. PCR reactions were set up in triplicate for all genes and contained 5 μl PCR buffer A, 4 mM MgCl<sub>2</sub>, 200 μM each of dATP, dGTP, dCTP and 400 μM dUTP, 250 nM fluorogenic probe (for RNR1: 5' TGA-TCT-CAA-AAA-GTG-CTG-GAG-GAA-TCG-GT 3'), 0.5 U UNG, 1.25 U AmpliTaq Gold, 16.75 μl H<sub>2</sub>O, 300 nM of appropriate FORWARD (for RNR1: 5' CGA-CAC-TTT-GAA-ATC-GTG-TGC-T 3') and REVERSE (for RNR1: 5' GCA-CCG-GTA-GAA-CGA-ATG-TTG 3') PCR primers, 1 μl of the RT reaction mixture. For the NAC, 1 μl of the 1:4 diluted RTase-negative sample was added while 1 μl of H<sub>2</sub>O was added to each non-template control sample. The ABI PRISM 7700 was run for 50 cycles of 15 s at 95°C, 1 min at 60°C. These cycles were preceded by 5 min at 50°C (UNG activation) and 10 min at 95°C (UNG inactivation and DNA denaturation). Data were analyzed using the ABI PRISM 7700 software package. Data were normalized according to ACT1 C<sub>T</sub>.

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values.

#### Library screening

Using primers 5pGalNistPCR and 3pGalNistPCR, a 0.6 kb  
5 region of the *C. albicans* SAM2 gene was PCR-amplified  
from a SAM2/pGAL1pNiST-1 construct isolated from clone  
36 and labeled with [<sup>32</sup>P]dCTP using the Multiprime™  
random-primed labeling system (Amersham). *C. albicans*  
genomic DNA isolated from strain B2630 was partially  
10 digested with Sau3AI, resolved on a 0.7% agarose gel  
and the region of the gel with the fragment size of  
interest (10-23kb) was cut out and DNA was eluted from  
the gel with Sephaglass Band Prep kit (Pharmacia). A  
*C. albicans* library in pYCP50 was prepared by ligating  
15 these fragments into a BamHI cut and dephosphorylated  
pYCP50 vector in a 1:2 molar ratio vector to insert.  
The titer (#colonies/μg DNA) was determined by  
transforming a fraction of the library to *E. coli*.  
Five genome equivalents were plated out and filter-  
20 lifts were prepared as described (Sambrook et al.,  
1989). Duplicate nylon filters were pre-washed for 2  
hours at 42°C in 50 mM Tris, 1M NaCl, 0.1% SDS, 1 mM  
EDTA to reduce background hybridization. The filters  
were subsequently hybridized at 42°C overnight in 5x  
25 SSPE, 50% formamide, 5x Denhardt's solution, 0.1% SDS,  
100 μg/ml denatured salmon sperm DNA and 10<sup>6</sup> cpm/ml of  
denatured probe. Filters were then washed in 2x SSC,  
0.5 % SDS for 1 hour at room temperature and for 1  
hour at 50°C. A few intense autoradiographic spots  
30 were found and the corresponding colonies were  
selected for plasmid preparation. Candidate clones  
were digested with a panel of restriction enzymes,  
resolved on a 0.7 % agarose gel, stained with  
ethidiumbromide and transferred to nylon membrane by  
35 vacuum-blotting. The blot was probed under the same  
conditions as the genomic library. A 1.1 kb HpaI



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fragment covering the entire hybridizing segment was subcloned into pCR-Blunt (Invitrogen)

5       **Screening for compounds modulating expression of polypeptides critical for growth and survival of *C. albicans***

          The method proposed is based on observations (Sandbaken et al., 1990; Hinnebusch and Liebman 1991; Ribogene PCT WO 95/11969, 1995) suggesting that  
10       underexpression or overexpression of any component of a process (e.g. translation) could lead to altered sensitivity to an inhibitor of a relevant step in that process. Such an inhibitor should be more potent against a cell limited by a deficiency in the  
15       macromolecule catalysing that step and/or less potent against a cell containing an excess of that macromolecule, as compared to the wild type (WT) cell.

          Mutant yeast strains, for example, have shown that some steps of translation are sensitive to the  
20       stoichiometry of macromolecules involved. (Sandbaken et al.). Such strains are more sensitive to compounds which specifically perturb translation (by acting on a component that participates in translation) but are equally sensitive to compounds with other mechanisms  
25       of action.

          This method thus not only provides a means to identify whether a test compound perturbs a certain process but also an indication of the site at which it exerts its effect. The component which is present in  
30       altered form or amount in a cell whose growth is affected by a test compound is potentially the site of action of the test compound.

          The assay to be set up involves measurement of growth of an isogenic strain which has been modified  
35       only in a certain specific allele, relative to a wild type (WT) *C. albicans* strain, in the presence of R-

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compounds. Strains can be ones in which the expression of a specific essential protein is impaired upon induction of anti-sense or strains which carry disruptions in an essential gene. An in silico approach to finding novel essential genes in *C. albicans* will be performed. A number of essential genes identified in this way will be disrupted (in one allele) and the resulting strains can be used for comparative growth screening.

10

Assay for High Throughput screening for drugs  
35  $\mu$ l minimal medium (S medium + 2% galactose + 2% maltose) is transferred in a transparent flat-bottomed 96 well plate using an automated pipetting system (Multidrop, Labsystems). A 96-channel pipettor (Hydra, Robbins Scientific) transfers 2.5  $\mu$ l of R-compound at  $10^{-3}$  M in DMSO from a stock plate into the assay plate.

20 The selected *C. albicans* strains (mutant and parent (CAI-4) strain) are stored as glycerol stocks (15%) at  $-70^{\circ}\text{C}$ . The strains are streaked out on selective plates (SD medium) and incubated for two days at  $30^{\circ}\text{C}$ . For the parent strain, CAI-4, the medium is always supplemented with 20  $\mu\text{g/ml}$  uridine. A single colony is scooped up and resuspended in 1 ml minimal medium (S medium + 2% galactose + 2% maltose). Cells are incubated at  $30^{\circ}\text{C}$  for 8 hours while shaking at 250 rpm. A 10 ml culture is inoculated at 250.000 cells/ml. Cultures are incubated at  $30^{\circ}\text{C}$  for 24 hours while shaking at 250 rpm. Cells are counted in Coulter counter and the final culture (S medium + 2% galactose + 2% maltose) is inoculated at 20.000 to 50.000 cells/ml. Cultures are grown at  $30^{\circ}\text{C}$  while shaking at 250 rpm until a final PD of 0.24 (+/- 0.04) 6nM is reached.

35

200  $\mu$ l of this yeast suspension is added to all

wells of MW96 plates containing R-compounds in a 450  $\mu$ l total volume. MW96 plates are incubated (static) at 30°C for 48 hours.

Optical densities are measured after 48 hours.

5           Test growth is expressed as a percentage of positive control growth for both mutant (x) and wild type (Y) strains. The ratio (x/y) of these derived variables is calculated.

## 10 RESULTS

A *C. albicans* integrative vector, pGAL1PSiST-1, was constructed to allow non-directional cloning of *C. albicans* genomic DNA fragments (Figure 2). The vector contains an inducible GAL1 promoter, a SfiI-cloned stuffer fragment, a *C. albicans* URA3 selection marker and elements to allow autonomous replication and selection in *E. coli*. A *C. albicans* genomic DNA library was prepared by ligating small genomic DNA fragments (400 to 1000 bp) which were linked to SfiI adaptors into the SfiI opened vector pGAL1PSiST-1 vector. Genomic DNA fragments (450 ng) were ligated into the pGAL1PSiST-1 vector (20 ng). After electroporation into *E. coli* approximately 400,000 clones were obtained. Plasmid DNA was prepared of ... clones; 91% contained an insert with an average length of 600 bp. The size of the library corresponds to over 5 times the diploid genome with genomic DNA inserts oriented in sense or antisense direction in the vector.

A similar *C. albicans* integrative vector, pGAL1PNiST-1, was constructed to allow SfiI/Not I directional cloning of *C. albicans* cDNA fragments (Figure 2). The SfiI/NotI cDNA was purified and sized on a Biogel column A150M. The first fraction contained approximately 38,720 clones upon transformation to *E. coli* with an average insert size of 1500 bp. cDNA from this fraction was ligated into a NotI/SfiI opened pGAL1PNiST-1 vector.

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C. albicans strain CAI-4 was transformed with the  
aforementioned genomic and cDNA libraries. Upon  
homologous recombination between the insert (partial or  
complete gene) in a library clone and the corresponding  
5 gene in the Candida genome, this gene is (partially if  
the gene is not full-length) duplicated (Figure 1). The  
first copy of the gene is flanked upstream by its native  
promoter and downstream by the GAL1 promoter. The  
direction of transcription from the native promoter is  
10 opposite to that of the GAL1 promoter. Induction of the  
GAL1 promoter might thus lead to altered expression of  
the gene at the integration site. Moreover, if the cDNA  
does not contain the entire 5' coding region, the first  
copy of the gene may not give rise to any more to a  
15 functional protein. The second copy of this gene has  
lost its promoter and will therefore not be transcribed  
(Figure 1).

Upon integration at the site of the GAL1 promoter,  
the promoter is duplicated yielding an integrated gene  
20 fragment under control of the GAL1 promoter (Figure 1).

Growth curves were measured in the presence of  
lithium acetate. Figure 3 shows growth curves of the  
wild type CAI-4 strain and transformants -resulting from  
cDNA library transformation- showing either an overall  
25 impaired growth (clone 38; Figure 3C) or galactose-  
induced (clone 36; Figure 3B) reduction in growth. This  
analysis was performed in S-glucose medium as a non-  
induction medium and S-galactose medium as an induction  
medium. The results shown in Figure 3A show that also  
30 the wild type strain shows reduced growth in antisense  
induction medium. This is because galactose is used  
rather inefficiently as a carbon source by C. albicans.  
In order to solve this problem and facilitate the  
selection procedure an extra carbon source, maltose, was  
35 added to both inducing and non-inducing medium. Again  
growth patterns varied significantly from transformant  
to transformant but growth of the parental strain CAI-4

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was nearly identical in both media (Figure 3D). Strains impaired in growth upon promoter activation showed a clear shift in the growth curve in medium supplemented with both galactose and maltose (clone 415; Figure 3E).  
5 Overall impaired growth was, as expected, not strongly influenced by the addition of maltose (clone 360; Figure 3F).

To verify that maltose as an extra carbon source did not affect the strength and inducibility of the GAL1 promoter, promoter activity was measured using  
10 *Kluyveromyces lactis* LAC4 reporter gene expression. CAI-4 was transformed with LAC4/pGAL1pNiST-1. Four individual transformants (named Q, R, S, T) were grown in glucose, galactose, glucose+maltose and  
15 galactose+maltose media and  $\beta$ -galactosidase activity was measured (Figure 4). It is clear that the presence of maltose does not significantly influence the induction ratio of the GAL1 promoter.

From a total of over 2000 transformants screened,  
20 198 (~10%) showed an impaired growth phenotype and were selected for further analysis. Forty-three % of these slow growers showed a growth pattern corresponding with a putative promoter interference or antisense effect, 57% showed overall impaired growth. PCR analysis with  
25 5pGALNiSTPCR and 3pGALNiSTPCR primers on genomic DNA from the transformants can reveal integration outside the gene showing sequence identity with the insert DNA, eg. at the GAL1 promoter region (Figure 1). Of all transformants screened by PCR using these primers,  
30 ~ 11% showed integration at a non-insert location.

When the insert of an antisense library clone recombines with the homologous gene in the *C. albicans* genome, no PCR product can be obtained upon amplification with 5pGALNiSTPCR and 3pGALNiSTPCR primers  
35 on genomic DNA (Figure 1). To release the plasmid from the genome and determine the integration site, genomic DNA was isolated from the transformants, cut (with SacI

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for the genomic library transformants and with PstI for the cDNA library transformants), religated and the resulting ligation reaction was precipitated and used as a template for inverse PCR. This procedure reveals homologous integration at the insert site as well as the number of integrations (assuming PCR products are of different lengths) within the *Candida* genome. This analysis was performed on all selected transformants, ~32 % of which showed multiple integrations. The frequency of multiple integrations was very variable and depended on the batch of transformants analyzed. The resulting PCR products from both analyses were subsequently sequenced and the sequences by compared with both public and proprietary sequence databases. In total 86 different genes could be identified, 45 of which were of unknown function.

For the CAI-4 transformants obtained with a genomic (non-directionally cloned) library, 26% of the selected clones (n=~150) contained the *C. albicans* autonomous replicating sequence, ARS2, and 15% of the clones contained a ribosomal RNA fragment.

For the CAI-4 transformants obtained with a cDNA library (n=~1850) a whole series of different gene fragments was found. As expected, also a number of genes involved in carbon source metabolism and nutrient uptake were identified.

Two examples of identified genes will be discussed, although as seen in Figures 16 to 70 similiar results were obtained for all of the sequences according to the invention. Clone 36 shows a galactose-induced impairment in growth, suggestive of a promoter interference or antisense effect (Figure 3B). In this clone recombination had occurred at the insert site as shown by amplification of a ~600bp gene fragment by inverse PCR. The s quence of the isolated gene fragment was 74 % identical to a *S. cerevisiae* S-adenosyl methionine synthetase 2 (SAM2) gene. Effects on SAM2 mRNA were

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assessed by Northern blots on total RNA extracted from a non-transformed control strain and from clone 36 grown either in antisense-inducing or non-inducing media. The Northern blot was hybridised with an in vitro synthesized SAM2 RNA sense probe to detect antisense transcripts (Figure 5). An identical Northern blot was hybridised with an in vitro synthesized SAM2 antisense probe to detect SAM2 mRNA (Figure 5). Both blots were subsequently hybridized with a TEF3 DNA probe to allow normalization. As the sequence of the *C. albicans* SAM2 gene was not available at the time, a *C. albicans* genomic library in pYcp50 was prepared and *E. coli* transformants were screened for the full-length gene using the 600 bp SAM2 PCR fragment as a probe. A strongly hybridizing clone was identified and designated clone 36.13.1. This clone contained the complete ORF (1155 bp) of the SAM2 gene including 5' and 3' flanking regions. In the very A/T-rich 5' flanking region a putative TATA box could be identified at -27 bp. The 3' flanking region contains multiple T-rich (>10 bp) regions, elements described in yeast as necessary for transcript release (Reeder and Lang, 1997). The complete SAM2 mRNA transcript thus has a predicted length of 1.2 kb.

Clone 38 showed impaired growth in both non-inducing and inducing media (Figure 3); this is expected when integration of the library plasmid itself leads to gene suppression. Clone 38 contained a 340 bp fragment of the ribonucleotide reductase 1 (RNR1) gene. RNR1 mRNA levels were analysed by Northern blot and quantitative PCR in a non-transformed control strain and clone 38 grown in S+glucose medium. The Northern blot was hybridised successively with an actin and an RNR1 doublestranded DNA probe (Figure 6). Although the  $\beta$ -actin transcript level in the control strain is lower compared to clone 38, the relative amount of RNR1 transcript is higher, indicating a reduced level of RNR1

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transcript in clone 38. This result was confirmed by Tagman quantitative PCR on both control strain and clone 38 using a RNR1 fluorogenic probe. Resulting Ct values were calculated and normalised for  $\beta$ -actin (Figure 6).  
5 Again RNR1 transcript levels in clone 38 were found reduced compared to the control strain.

To verify that the growth-effect was due to the interference with the identified gene and to support the specificity of the antisense effect, single allele knock-  
10 outs were made in 6 identified genes using the URA-blaster method (Fonzi and Irwin, 1993). Disruption of one allele of a gene should in theory lead to ~ 50 % reduction in gene transcript. In practice however we have observed reductions varying between 10 and 100 %  
15 of normal level. This can probably be explained by the fact that not always both copies of a gene are functional. That only a single integration at the correct site had occurred for each of the disruption cassettes was verified by PCR and Southern blot  
20 analysis. Growth curves were measured; three disruptants showed impaired growth, suggesting that a gene required for growth or survival was targeted. Experiments to take over control of the second allele of each gene -by promoter replacement- are ongoing.

25 The present application describes new methods to diminish endogenous gene expression in the medically important yeast *C. albicans*. Our approach proved very useful for the identification of genes required for growth or survival. Technical hurdles consisted of the  
30 lack of an efficient transformation method for *C. albicans* (Logghe M., submitted) and the need to measure growth reproducibly on a large number of transformants in parallel. The latter was achieved with a Bioscreen Analyzer (LabSystems) which can simultaneously measure  
35 growth in 200 cultures and subsequently generate growth curves automatically. Although in principle this kind of screening could be done on plates we could not



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achieve satisfactory reproducibility using plate screening.

5 In our genomic screen, integration of the library  
plasmid can happen either at the endogenous GAL1  
promoter locus or, more frequently, at the locus  
10 corresponding to the plasmid insert. The latter results  
in a gene duplication with the first copy of the gene  
flanked by two convergently oriented promoters. The use  
of such a "collision construct" has previously been  
described in screening for inhibitors of transcriptional  
15 activation in mammalian cells (patent WO 97/10360; Giese  
K.). If RNA polymerase II complexes start from both the  
upstream and downstream, oppositely oriented, promoter  
regions, they may collide thereby preventing the  
formation of a full-length mRNA transcript. The second  
20 copy of the gene has no more a promoter and is probably  
5' crippled as the original inserts cloned into the  
library have an average length of ~1.5 kb while ORFs in  
*C. albicans* have an average length of ... and we ourselves  
identified ORFs of (unknown) genes larger than 7 kb.

Upon integration of a plasmid into the *C. albicans*  
genome, reduced function of the protein encoded by the  
disrupted gene can be due to several mechanisms: 1) The  
25 first copy of the duplicated gene can be prevented from  
forming functional sense transcript by promoter  
collision or the sense transcript may be inhibited by  
true antisense. Indeed, although a 1.2 kb SAM2  
antisense transcript could be detected in clone 36 we  
cannot exclude the growth defect being due to promoter  
30 interference. If an antisense transcript is formed from  
an intact SAM2 gene, we expect a transcript of at least  
1055 bp; no transcription terminator was engineered  
upstream of this gene so transcription will proceed  
until an appropriate transcription termination  
35 recognition site is reached. The promoter region of the  
SAM2 gene is particularly A/T rich and contains a  
reversed yeast transcription terminator site at - 118

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(with translation starting at +1). In yeast, transcription terminator sites are ill-defined but for a T-rich stretch with non-T residues situated appropriately to prevent slippage (Jeong et al., 1996; Reeder and Lang, 1997). If termination of transcription occurs at this theoretically predicted site, a 1.17 kb transcript would be expected, as was found. 2) If mutations were present in the original library clone, the protein encoded by the gene after homologous recombination could be non-functional. 3) Possible cis down-regulatory effects on adjacent genes could be induced upon integration of large DNA fragments at certain locations within the genome. 4) Finally, gene disruption could occur by recombination with cDNA that is not full-length at the 5' end.

If -on the contrary- integration happens at the endogenous GAL1 promoter site, the GAL1 promoter is duplicated and antisense can be induced from this promoter. Promoter collision is not possible as the endogenous promoter of the gene is lacking at the integration site. Integration at a non-homologous site within the genome is rare. Transformation efficiencies of 0.7-3 transformants/ $\mu$ g have been reported upon transformation of CAI-4 with non-homologous plasmid DNA (Thompson et al., 1998). Also, integration at the URA3 locus is very unlikely as the complete URA3 gene has been removed from the CAI-4 genome.

Irrespective of the mechanism responsible for gene suppression, we could identify genes required for growth or survival by screening for transformants showing either galactose-induced or complete growth block. Furthermore, for such genome-wide screening no prior sequence information is needed and it allows discovery of possibly new critical functions. However, some genes may only be critical under conditions different from growth in minimal medium (as used in our screening) e.g. environments with high oxygen tension, high osmolarity

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or high pH. However, it would be possible to screen for a growth phenotype under these conditions using our screening method. Alternatively, some genes may play critical roles only under unusual growth states or may specifically be required for adaptation to conditions encountered during infection of a host.

More than half of the ORFs we have identified as being critical for growth have a completely unknown function. Even though required for growth in *C. albicans*, for some genes no homologues could be found in existing databases, suggesting that they are species-specific genes. Indeed, recent genome sequencing efforts (e.g. *Mycoplasma genitalium* (Fraser et al., 1995), *Haemophilus influenzae* (Fleischmann et al., 1995)) have shown that approximately 20 % of the predicted ORFs in a microbial genome can be species-specific.

One disadvantage of the technique is that multiple library plasmids can integrate in the genome of a single *C. albicans* cell. When this occurs, identification of the target responsible for the growth defect becomes more difficult. Also, as shown in *Schizosaccharomyces pombe* (Atkins et al., 1995), RNA-mediated suppression may not be effective for certain genes, which we would miss when relying only on this technique.

Rather unexpectedly, transformation with the genomic library and subsequent screening for transformants showing reduced growth frequently yielded ARS2- and rRNA-containing clones (in 26 and 15% respectively of the transformants showing reduced growth). Previously, a study of aging yeast mother cells had shown that accumulation of extrachromosomal rDNA circles (ERCs) occurs in old cells and that these ERCs actually cause aging (Sinclair et al., 1997; Johnson et al., 1999). rDNA is present at 100-200 tandem copies on chromosome XII of *S. cerevisiae* and was found to accumulate to about 1000 copies in senescent cells. One other gene we identified is a homologue of the

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essential *S. cerevisiae* gene TRAl, a protein kinase showing highest identity to the human TRRAP gene (McMahon et al., 1998) which is an ataxia telangiectasia mutated (ATM)-related gene. Loss of ATM is a genetic defect identified in ataxia telangiectasia (Johnson et al., 1999), a disease in humans where life span is typically reduced to 40-50 years. We might thus have picked up a number of growth-inhibitory effects due to induction of aging.

The strategy presented should be applicable to all organisms for which existing techniques for "en masse" gene disruption are not easily applicable because of their diploid nature and lack of sexual cycle and might prove especially useful for other diploid imperfect yeasts.

Although the genomic strategy that we described cannot substitute for a comprehensive investigation of individual genes and pathways, it can provide a good starting point for such investigation.

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**TABLE 1**

	<u>Seq ID No.</u>	<u>Clone</u>	<u>Function</u>
5	1	214c_cpL1	-
	2	113g2	-
	3	222g8	-
	4	222g8(prt)	-
10	5	222g9	-
	6	222g9_CDS_1	-
	7	222g9_CDS_2	-
	8	222g9_CDS_3	-
15	9	222g9_CDS_4	-
	10	24gG	-
	11	28gK	-
	12	328c1	-
20	13	328c1(prt)	-
	14	33gK	-
	15	33gK(prt)	-
	16	3gG	-
25	17	58gA	-
	18	21g2	-
	19	21g2(prt)	5' UTR TRA1
	20	223c_cp	CFL
30	21	357cl	
	22	357cl(prt)	RPL27
	23	110c_af	
	24	110c_af(prt)	SADH
35	25	CDC48	
	26	CDC48(prt)	CDC48
	27	99g3	
	28	99g3(prt)	CIT
40	29	ESP1	
	30	ESP1(prt)	ESP1
	31	190g3	
	32	190g3(prt)	FAL1
45	33	249c_af	
	34	249c_af(prt)	MAA
	35	485cl	
	36	485cl(prt)	RPL16
50	37	328c3	
	38	328c3(prt)	RPS21
	39	83c3	
	40	83c3(prt)	SHA3
	41	233c_cp2	
	42	233c_cp2	TP11
	43	214c_cpL1	HXT6_2
	44	128g4	15S rRNA
	45	135g	tRNA_Ser

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	<u>Seq ID No.</u>	<u>Clone</u>	<u>Function</u>
	46	22g3	
5	47	22g3_CDS1	
	48	22g3_CDS2	-
	49	38g1	-
	50	117c_af	-
	51	117c_af(prt)	-
10	52	17g1	-
	53	17g1_CDS1	-
	54	17g1_CDS2	-
	55	480c	-
	56	480c(prt)	-
15	57	55g3	-
	58	55g3(prt)	-
	59	61gB	
	60	61gB(prt)	PSP2
	61	62gB	
20	62	62gB(prt)	-
	63	80g3	
	64	80g3(prt)	-
	65	29g2_part1	
	66	29g2_part1(prt)	EF4
25	67	29g2_part2_3	
	68	29g2_part2(prt)	EF4
	69	29g2_part3(prt)	EF4
	70	226c_af2	
	71	226c_af2(prt)	ADE12
30	72	409c5	
	73	409c5(prt)	HOL1
	74	40c_af	
	75	40c_af(prt)	FBP
	76	55g1	
35	77	55g1(prt)	MEG1
	78	67g1	
	79	67g1(prt)	RVS187
	80	232c_cp	
	81	360c6	
40	82	360c6(prt)	HXT6_1
	83	98c_cp	
	84	98c_cp(prt)	KGD2
	85	17c_cp	
	86	17c_cp(prt)	NDE1
45	87	60gK	
	88	60gK(prt)	RAD18
	89	226c_af1	
	90	226c_af1(prt)	-
	91	328c2	
50	92	328c2(prt)	-
	93	498c_cp	

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	<u>Seq ID No.</u>	<u>Clone</u>	<u>Function</u>
5	94	498c_cp(prt)	-
	95	64gB	
	96	64gB(prt)	-
	97	8c_cp	
	98	8c_cp(prt)	-
10	99	15c1	
	100	15c1(prt)	-
	101	233c_cp1	
	102	233c_cp1_CDS1	
	103	233c_cp1_CDS2	-
15	104	35gK	
	105	35gK(prt)	-
	106	36g2	
	107	36g2(prt)	-
	108	65g	
20	109	65g(prt)	-
	110	85g3	
	111	85g3(prt)	
	112	232c_cp(prt)	SAP
	113	409c10	
25	114	409c10(prt)	-

**KNOCK-OUT DATA SHEET****A. FAL1 single allele knock-out**

Correct and single integration of FAL1 disruption cassette was confirmed by both PCR and Southern blot analysis (see support data on CD-ROM)

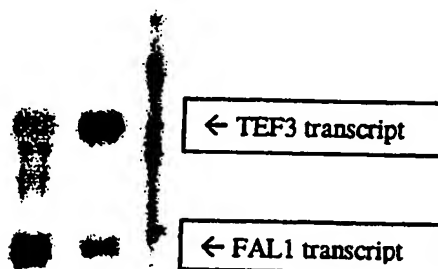
**1. Analysis on RNA level****Northern blot analysis:**

Lane 1: RNA MWM I (Boehringer Mannheim)

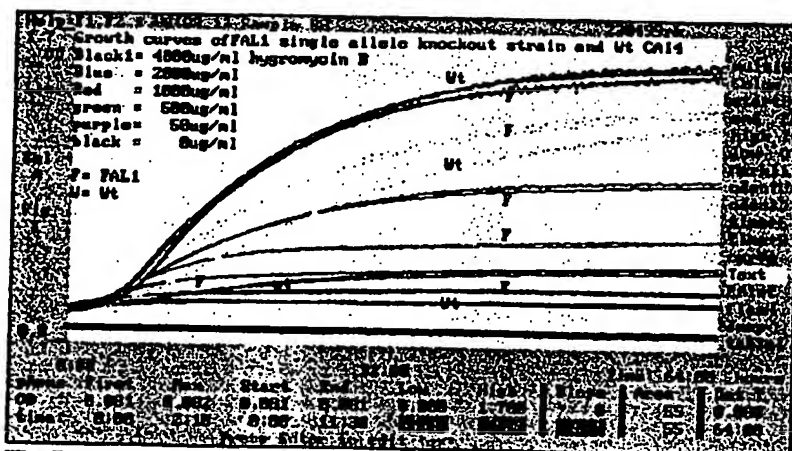
Lane 2: WT + gal + mal + LiAc

Lane 3: FAL1 + gal + mal + LiAc

Lane 4: RNA MWM I DIG labeled (Boehringer Mannheim)



Lower FAL1 transcript levels are observed in the FAL1 single allele knock-out strain compared to the wild type strain.

**2. Growth analysis**

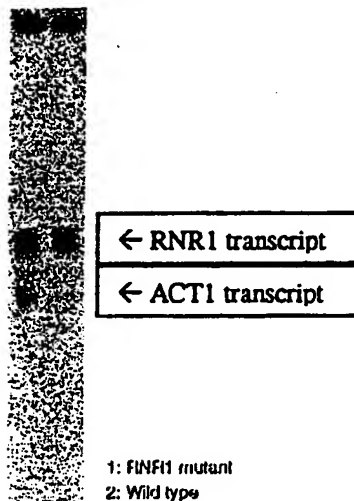
The FAL1 single allele knock-out grows equal to the wild type, however it is significantly more resistant to Hygromycin B.

## B. RNR1 single allele knock-out

Correct and single integration of RNR1 disruption cassette was confirmed by both PCR and Southern blot analysis (see support data on CD-ROM)

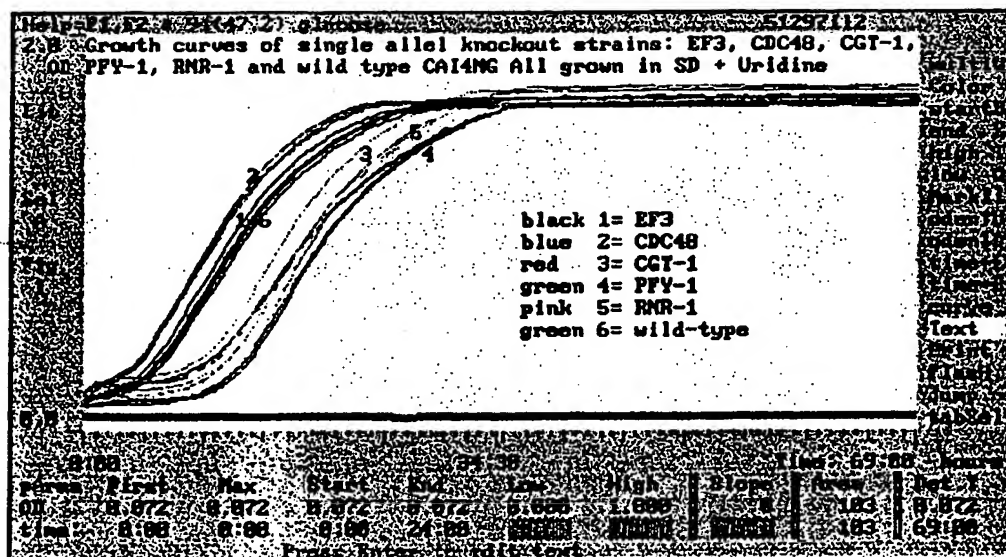
### 1. Analysis on RNA level

#### Northern blot analysis:



Lower RNR1 transcript levels are observed in the RNR1 single allele knock-out strain compared to the wild type strain. This result was confirmed by quantitative PCR (QT-PCR).

### 2. Growth analysis



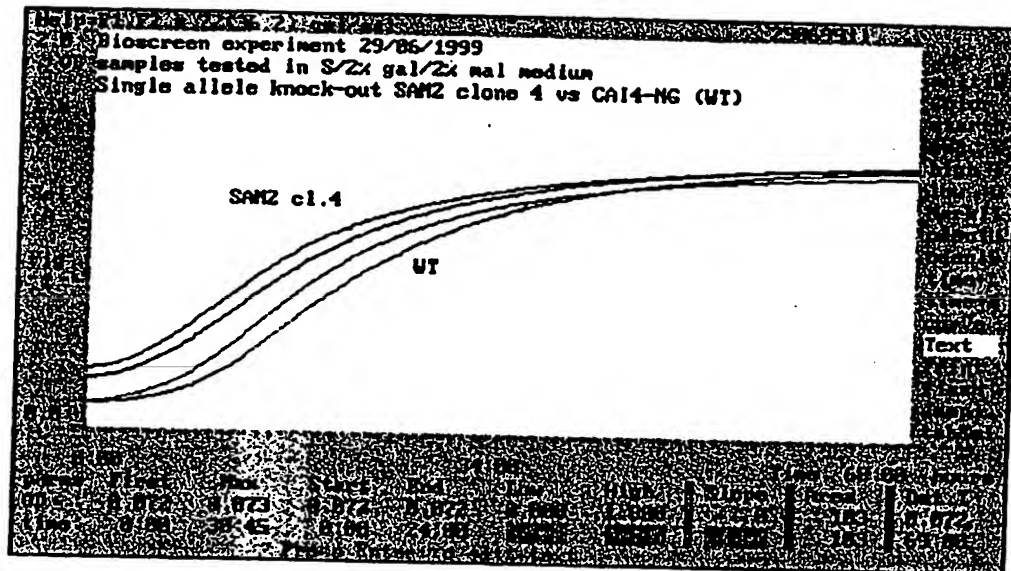
### C. SAM2 single allele knock-out

Correct and single integration of SAM2 disruption cassette was confirmed by both PCR and Southern blot analysis (see support data on CD-ROM)

#### 1. Analysis on RNA level

Northern blot analysis:

#### 2. Growth analysis



Inoculum for SAM2 was somewhat higher; at equal inocula growth of SAM2 single allele knock-out is slightly slower.



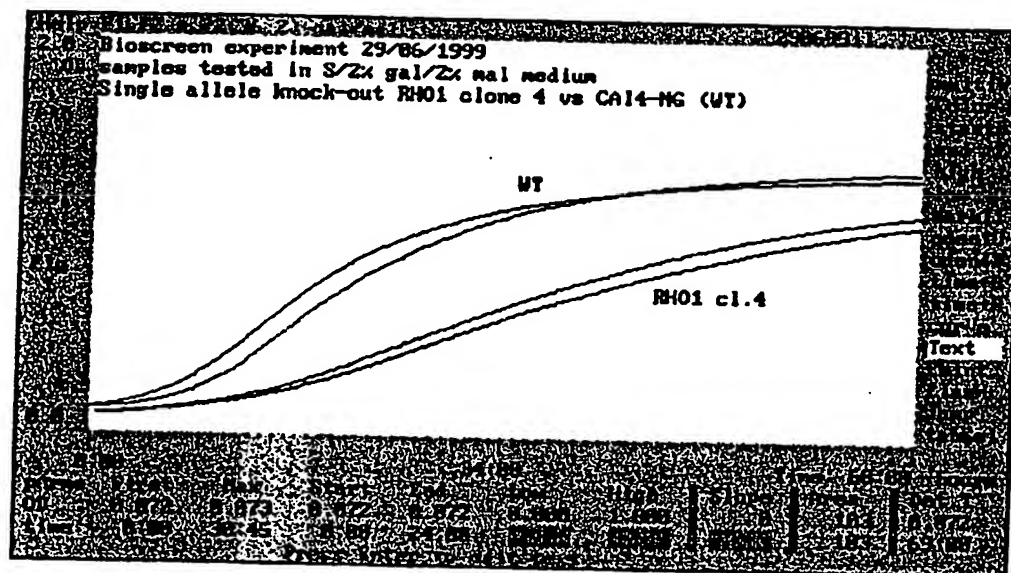
#### D. RHO1 single allele knock-out

Correct and single integration of RHO1 disruption cassette was confirmed by both PCR and Southern blot analysis (see support data on CD-ROM)

##### 1. Analysis on RNA level

Northern blot analysis:

##### 2. Growth analysis



Growth of the RHO1 single allele knock-out is impaired compared to wild type growth.

### E. MEG1 single allele knock-out

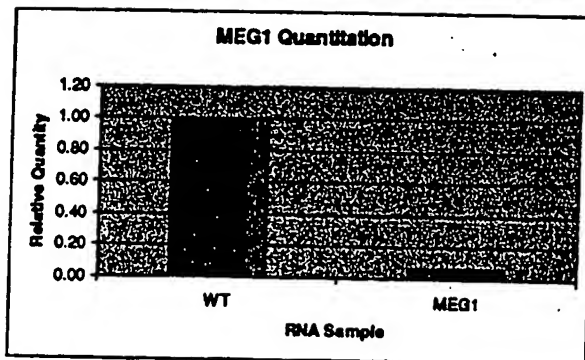
Correct and single integration of MEG1 disruption cassette was confirmed by both PCR and Southern blot analysis (see support data on CD-ROM)

#### 1. Analysis on RNA level

QT-PCR analysis:

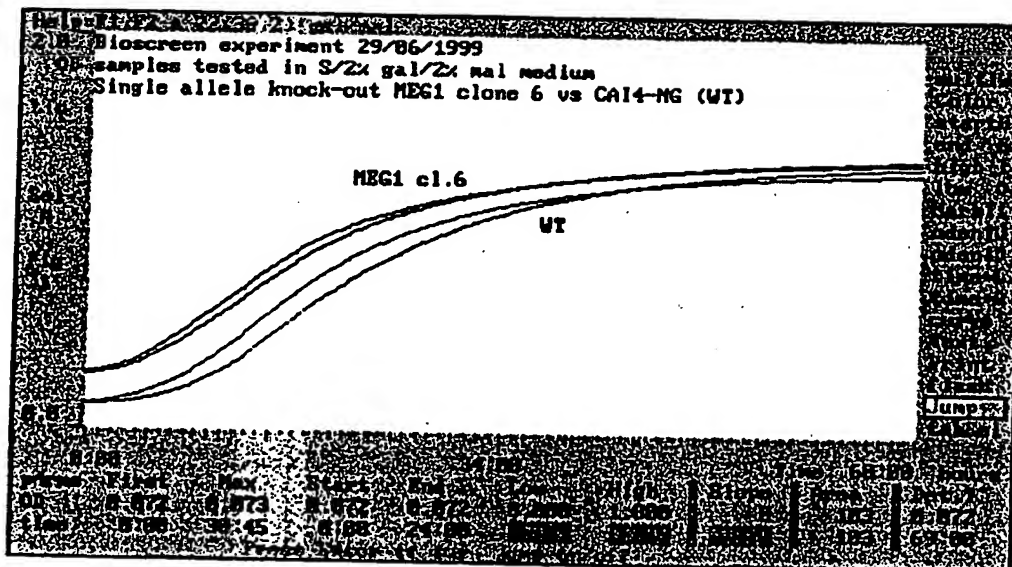
#### Relative quantitation for MEG1 vs. Act

	Avrg. MEG1	Avrg. ACT	dCt	ddCt	2-ddct
WT	35.79	33.49	2.29	0.00	1.00
MEG1	38.62	32.57	6.05	3.76	0.07



MEG1 expression was decreased more than 14 fold in the MEG1 single allele knock-out compared to the Wt.

#### 2. Growth analysis



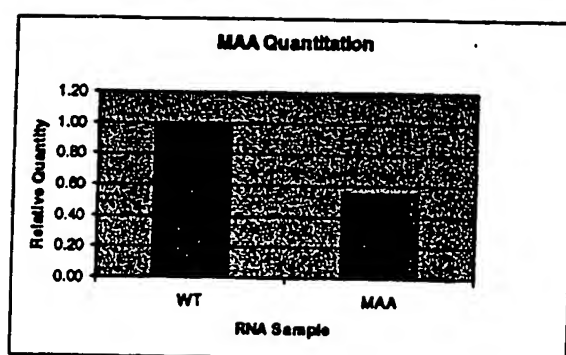
Inoculum for SAM2 was somewhat higher; at equal inocula growth of SAM2 single allele knock-out is slightly slower.

**F. MAA single allele knock-out**

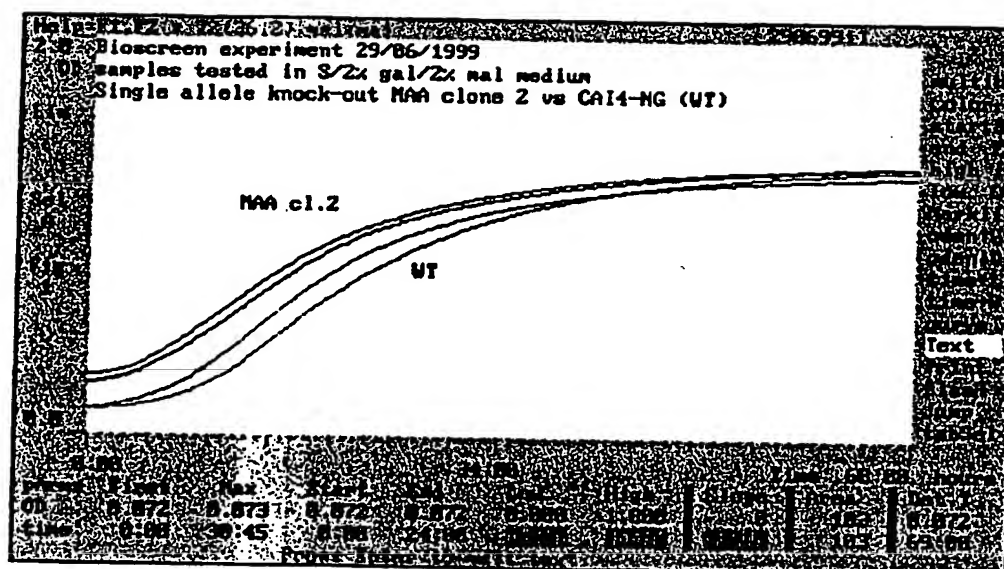
Correct and single integration of MAA disruption cassette was confirmed by both PCR and Southern blot analysis (see support data on CD-ROM)

**1. Analysis on RNA level****QT-PCR analysis:****Relative quantitation for MAA vs. Act**

	Avrg. MAA	Avrg. ACT	dCt	ddCt	2-ddct
WT	34.85	33.48	1.36	0.00	1.00
MAA	32.86	30.64	2.22	0.86	0.55



MAA expression was decreased two fold in the MAA knock-out compared to the Wt.

**2. Growth analysis**

Inoculum for MAA was somewhat higher; at equal inocula growth of MAA single allele knock-out is slightly slower.



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## Claims

1. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which nucleic acid molecule comprises any of the sequences of nucleotides in Sequence ID Numbers 1, 2, 3, 5, 10, 11, 12, 14, 16, 17, 18, 20, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 44, 45, 46, 49, 50, 52, 55, 57, 59, 61, 63, 65, 67, 70, 72, 74, 76, 78, 80, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 104, 106, 108, 110 and 113 or the sequences of nucleotides identified in Figures 9 to 13.
2. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which nucleic acid molecule comprises any of the sequences of nucleotides in Sequence ID Numbers 1, 2, 3, 5, 10, 11, 12, 14, 16, 17, 18, 46, 49, 50, 52, 55, 57, 59, 61, 63, 65, 87, 89, 91, 93, 95, 97, 99, 101, 104, 106, 108, and 110, or fragments or derivatives of said nucleic acid molecules.
3. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which nucleic acid molecule comprises any of the sequences of nucleotides in Sequence ID Numbers 20, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 45, 65, 70, 72, 74, 76, 78, 80, 81, 83, 85, 113, and fragments or derivatives of said nucleic acid molecules.
4. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which nucleic acid molecule comprises any of the sequences of nucleotides of sequence ID Nos 1 and 91.

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5. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which polypeptide has an amino acid sequence according to the sequence of any of Sequence ID Numbers 4, 6 to 9, 13, 15, 19, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 43, 47, 48, 51, 53, 54, 56, 58, 60, 62, 64, 66, 68, 69, 71, 73, 75, 77, 79, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 103, 105, 107, 109, 111, 112, and 114 or the sequences identified in Figures 14 and 15.

6. A nucleic acid molecule according to any one of claims 1 to 5 which is mRNA.

7. A nucleic acid molecule according to any of claims 1 to 5 which is DNA.

8. A nucleic acid molecule according to claim 7 which is cDNA.

9. A nucleic acid molecule capable of hybridising to the molecules according to any of claims 1 to 5 under high stringency conditions.

10. A nucleic acid molecule according to claim 9 which is an antisense molecule.

11. A polypeptide encoded by the nucleic acid molecule according to any of claims 1 to 8.

12. A polypeptide which is critical for survival and growth of the yeast *Candida albicans* having the amino acid sequences of any of Sequence ID Numbers 4, 6 to 9, 13, 15, 19, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 43, 47, 48, 51, 53, 54, 56, 58, 60, 62, 64, 66, 68, 69, 71, 73, 75, 77, 79, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 103, 105, 107, 109, 111, 112, and 114.

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13. A polypeptide according to claim 12 having an amino acid sequence of any of Sequence ID Numbers 4, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 66, 68, 69, 71, 73, 75, 77, 79, 82, 84, 86 and 114.

5

14. A polypeptide according to claim 12 having an amino acid sequence of any of Sequence ID Nos 43 or 92.

15. An expression vector comprising a nucleic acid molecule according to claim 7 or 8.

10

16. An expression vector according to claim 15 which comprises an inducible promoter.

15

17. An expression vector according to claim 15 or 16 which comprises a sequence encoding a reporter molecule.

18. A nucleic acid molecule according to any of claims 1 to 10 for use as a medicament.

20

19. Use of a nucleic acid molecule according to any of claims 1 to 10 in the preparation of a medicament for treating *Candida albicans* associated diseases.

25

20. A polypeptide according to any of claims 11 to 14 for use as a medicament.

21. Use of a polypeptide according to any of claims 11 to 14 in the preparation of a medicament for treating *Candida albicans* associated infections.

30

22. A pharmaceutical composition comprising a nucleic acid molecule according to any of claims 1 to 10 or a polypeptide according to any of claims 11 to 14 together with a pharmaceutically acceptable carrier diluent or excipient therefor.

35

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23. A *Candida albicans* cell comprising an induced mutation in the DNA sequence encoding a polypeptide according to any of claims 11 to 14.

5           24. A method of identifying compounds which selectively modulate expression of polypeptides which are crucial for growth and survival of *Candida albicans*, which method comprises:

- 10           (a) contacting a compound to be tested with one or more *Candida albicans* cells having a mutation in a nucleic acid molecule corresponding to the sequences according to any of claims 1 to 8 which mutation results in overexpression or underexpression of said polypeptides, in addition to contacting one  
15           or more wild type *Candida albicans* cells with said compound,
- (b) monitoring the growth and/or activity of said mutated cell compared to said wild type;  
20           wherein differential growth or activity of said one or more mutated *Candida* cells is indicative of selective action of said compound on a polypeptide or another polypeptide in the same or a parallel  
25           pathway.

25           25. A compound identifiable according to the method of claim 24.

30           26. A compound according to claim 25 for use as a medicament.

35           27. Use of a compound according to claim 25 in the preparation of a medicament for treating *Candida albicans* associated diseases.

            28. A pharmaceutical composition comprising a



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compound according to claim 24 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

5           29. A method of identifying DNA sequences from a cell or organism which DNA encodes polypeptides which are critical for growth or survival of said cell or organism, which method comprises:

- 10           (a) preparing a cDNA or genomic library from said cell or organism in a suitable expression vector which vector is such that it can either integrate into the genome in said cell or that it permits transcription of antisense RNA from the nucleotide sequences in said
- 15           cDNA or genomic library,
- (b) selecting transformants exhibiting impaired growth and determining the nucleotide sequence of the cDNA or genomic sequence from the library included in the vector from said
- 20           transformant.

30. A method according to claim 29 wherein said cell or organism is a yeast or filamentous fungi.

25           31. A method according to claim 29 or 30 wherein said cell or organism is any of *Saccharomyces cerevisiae*, *Saccharomyces pombe* or *Candida albicans*.

30           32. Plasmid pGAL1PSiST-1 having the sequence of nucleotides illustrated in Figure 8.

33. Plasmid pGAL1PNiST-1 having the sequence of nucleotides illustrated in Figure 7.

35           34. An antibody capable of binding to a polypeptide according to any of claims 11 to 14.

- 60 -

35. An oligonucleotide comprising a fragment of from 10 to 50 contiguous nucleic acid sequences of a nucleic acid molecule according to any of claims 1 to 10.

5

36. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans*, said nucleic acid molecule comprising the sequences of any of the nucleotide sequences illustrated in Figures 9 to 13.

10

37. A polypeptide which is critical for survival and growth of the yeast *Candida albicans*, said polypeptide comprising the amino acid sequences of any of the sequences illustrated in Figures 14 or 15.

15

38. A method of identifying for the presence of *Candida albicans* in a subject, which method comprises contacting a sample to be tested with nucleic acid molecule according to claim 10 or an antibody according to claim 34, and monitoring for any hybridisation with said molecule or binding to said antibody.

20

39. A kit for monitoring *Candida albicans* infection comprising a molecule according to claim 9 or 10, or an antibody according to claim 34, and means for contacting said molecule or said antibody with a sample to be tested.

25

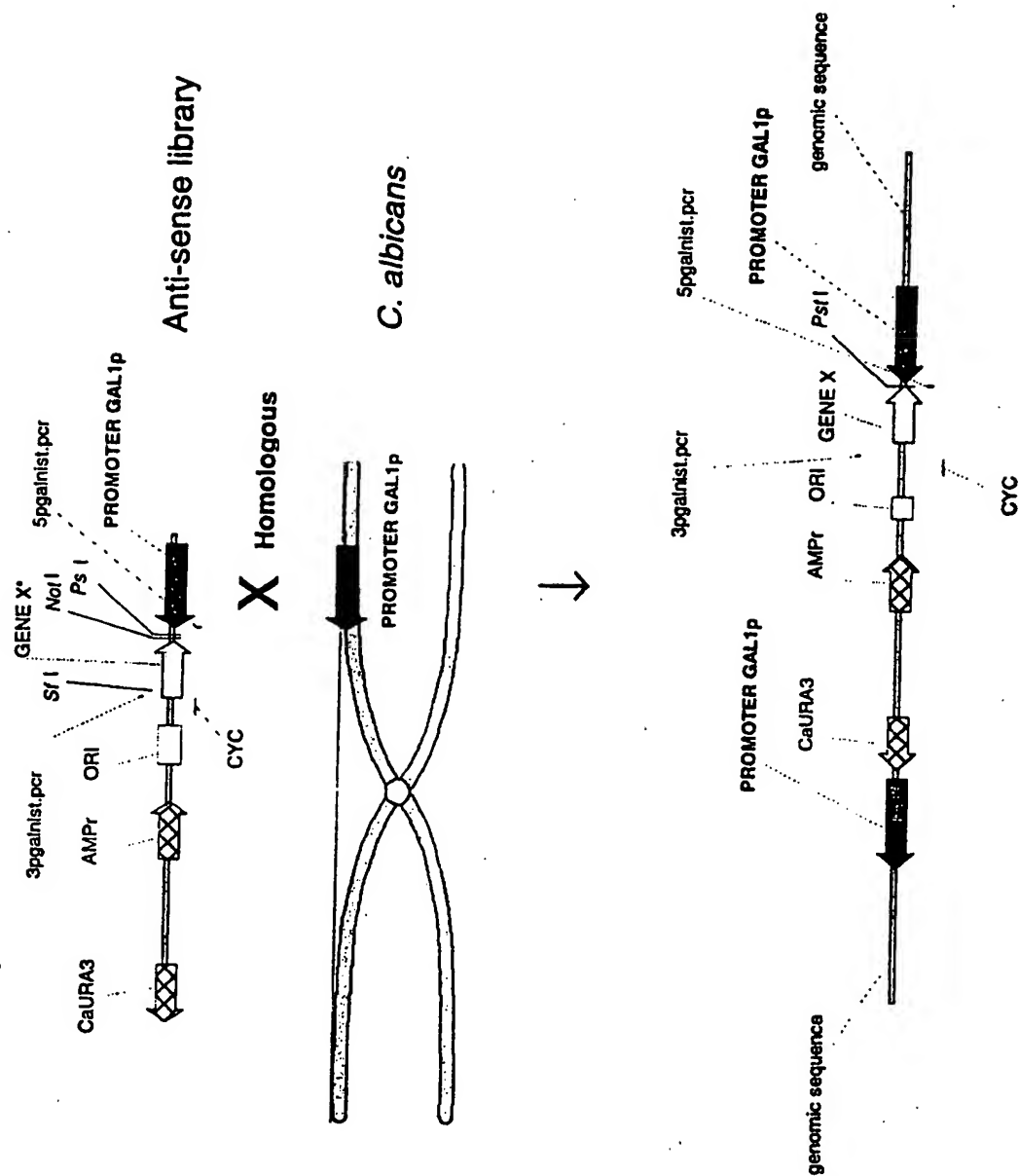
40. A nucleic acid molecule encoding a polypeptide which is critical for survival and growth of the yeast *Candida albicans* and which nucleic acid molecule comprises any of the sequences of nucleotides in Sequence ID Numbers 18, 21, 29, 31, 33, 44, 76, 80 and the sequences identified in Figures 9 and 13.

30

35

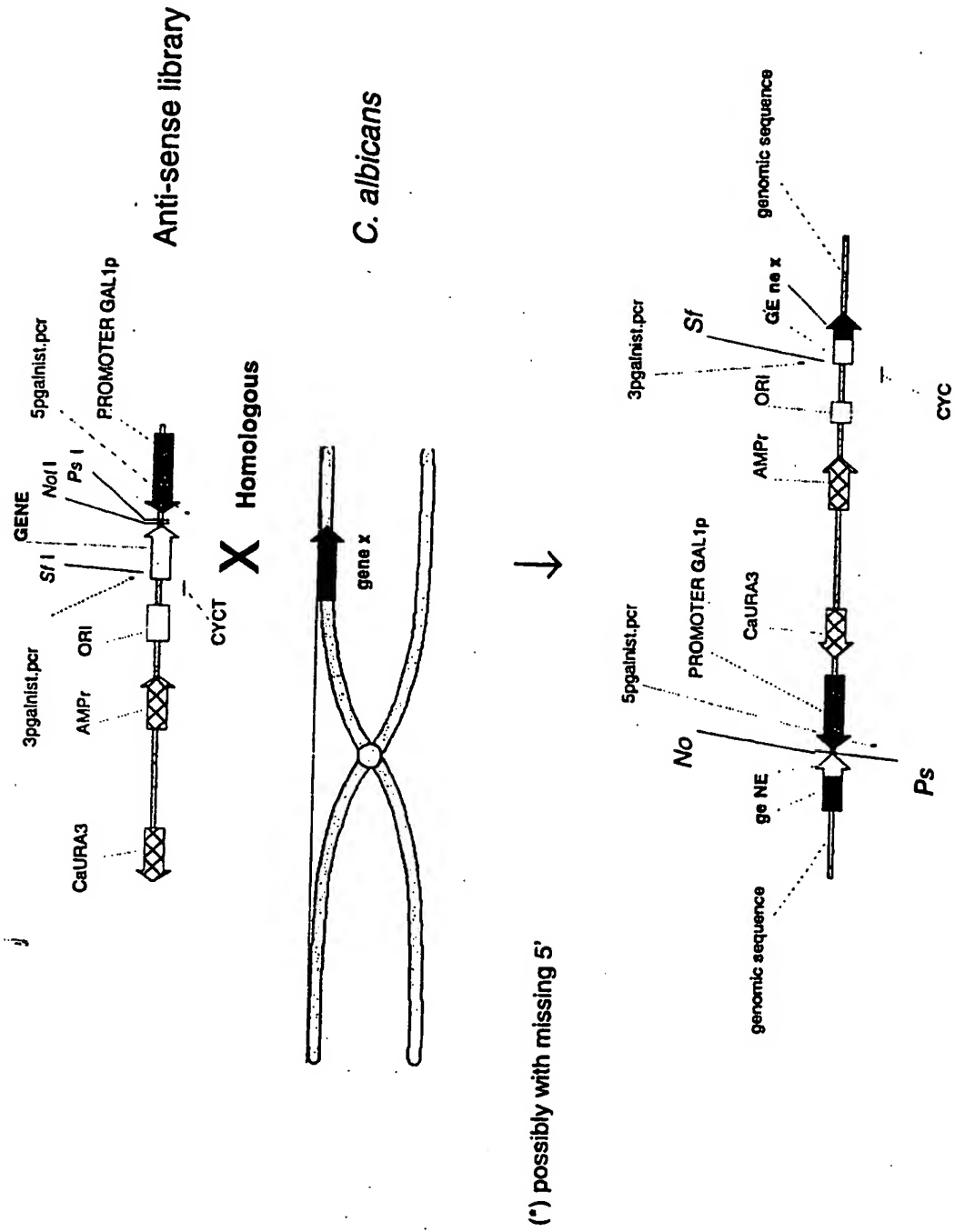
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Figure 1A:



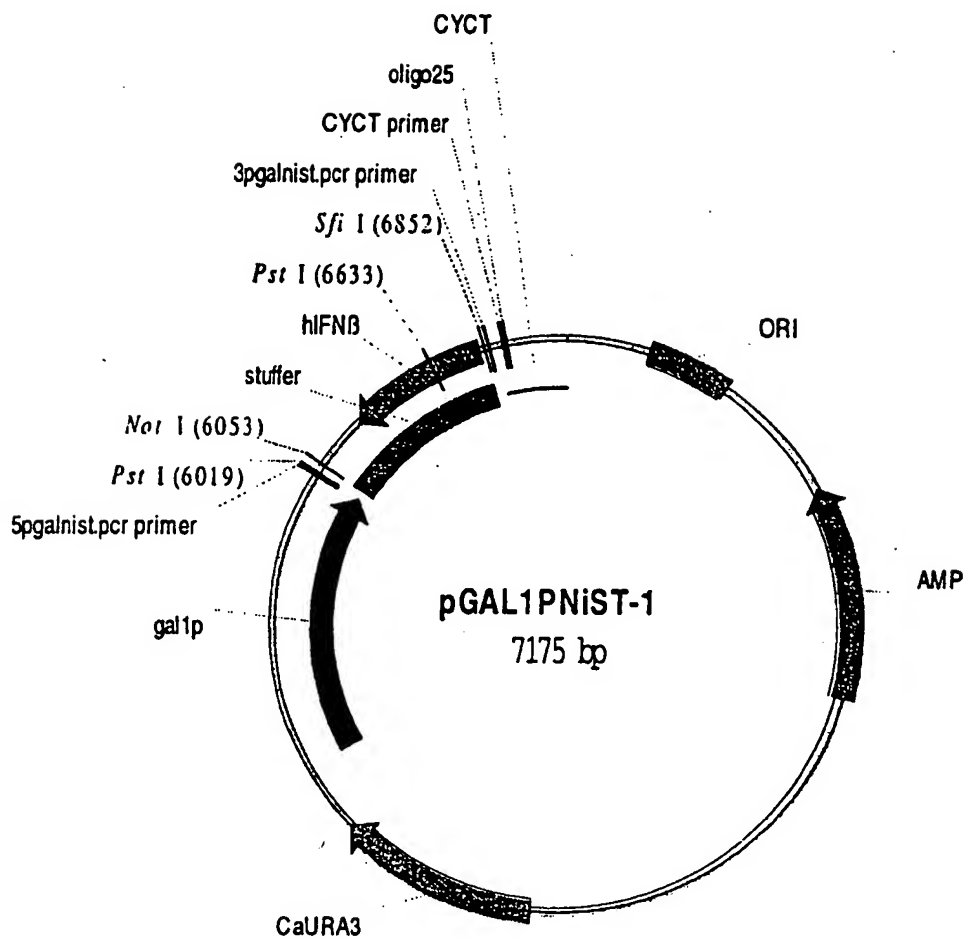
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Figure 1B:



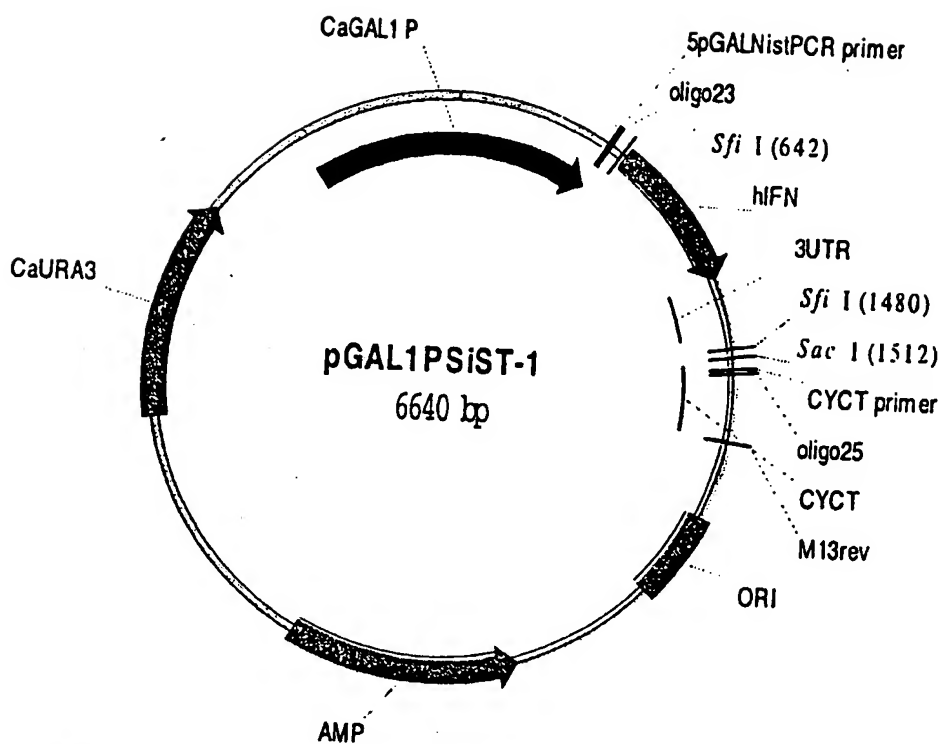
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FIG. 2(a)



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FIG. 2(b)



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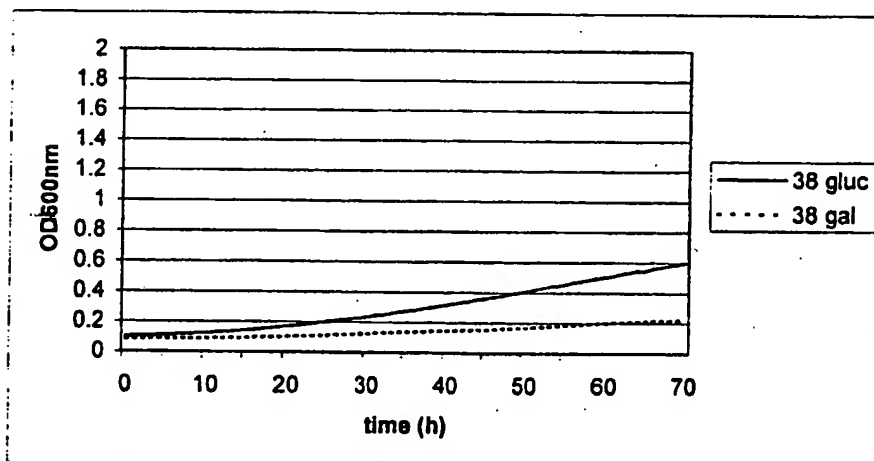
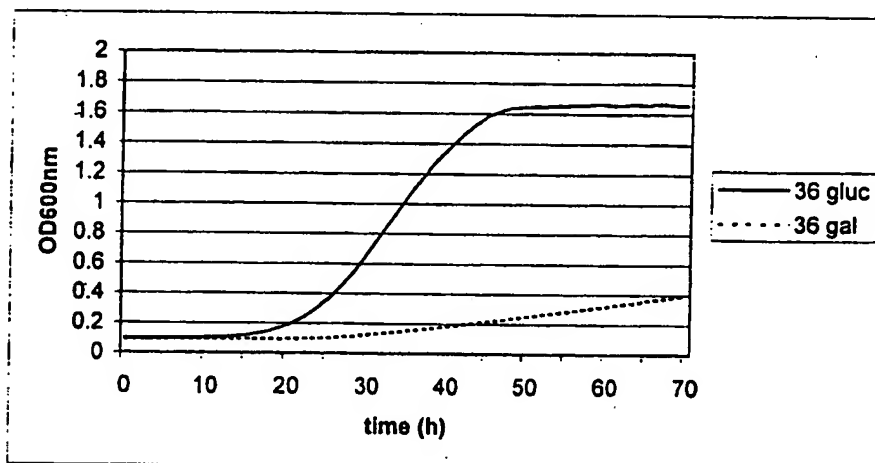
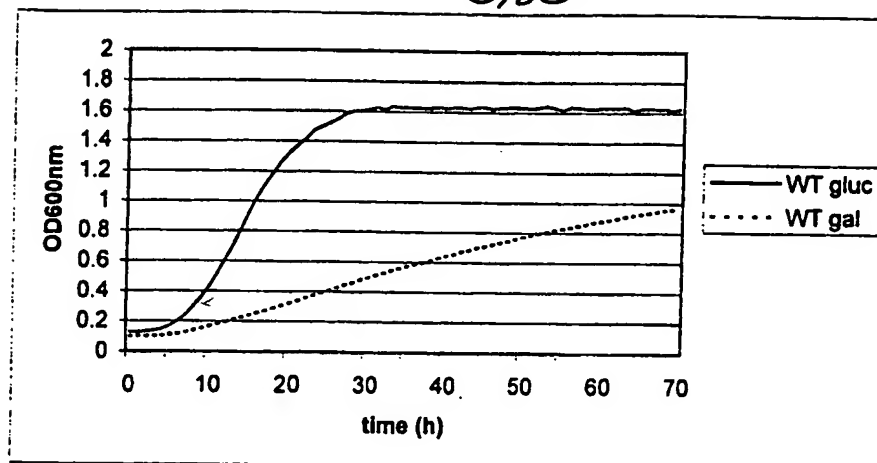


FIG. 3.

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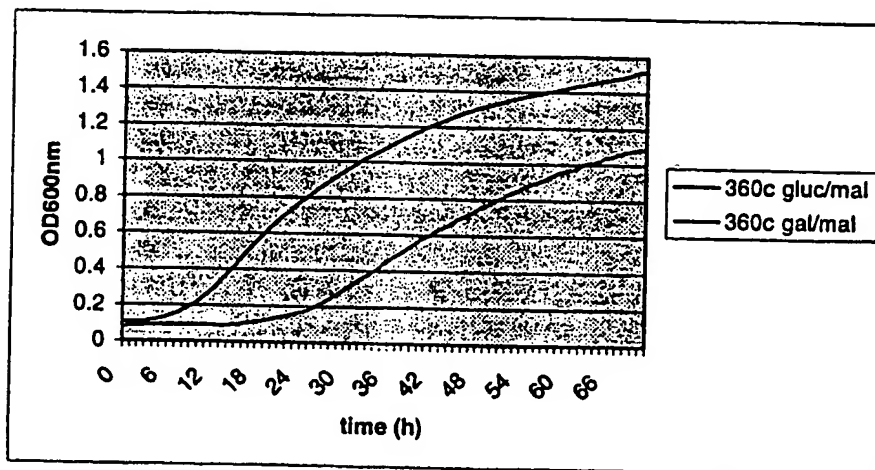
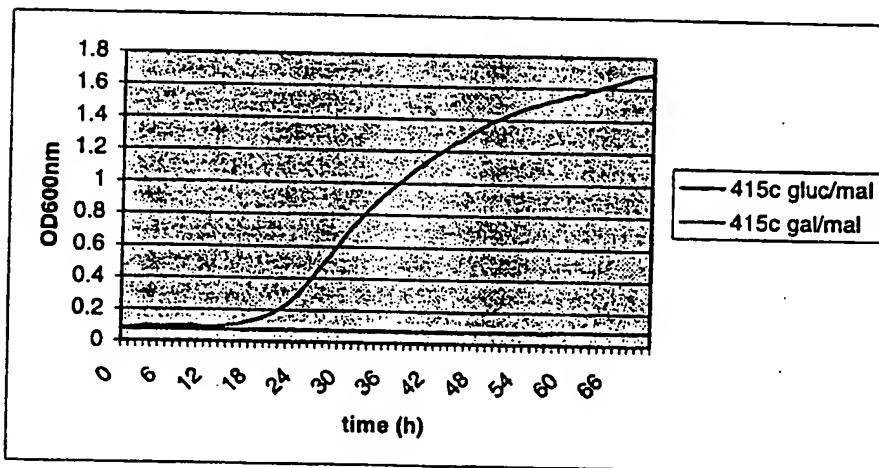
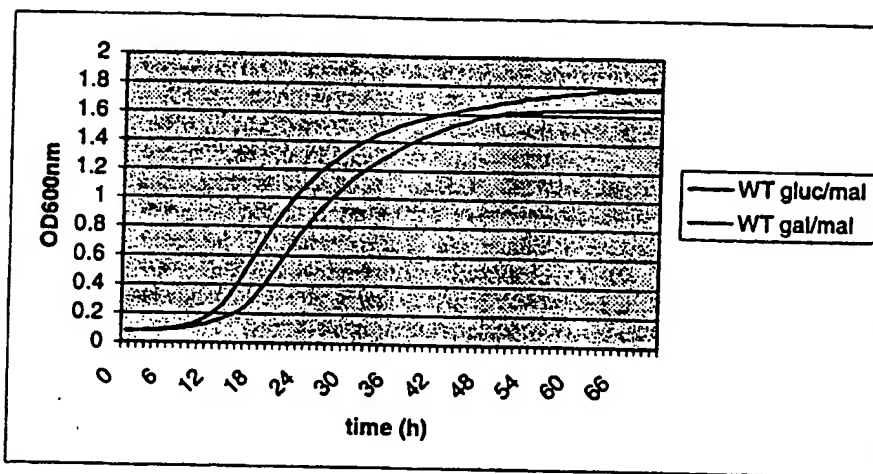


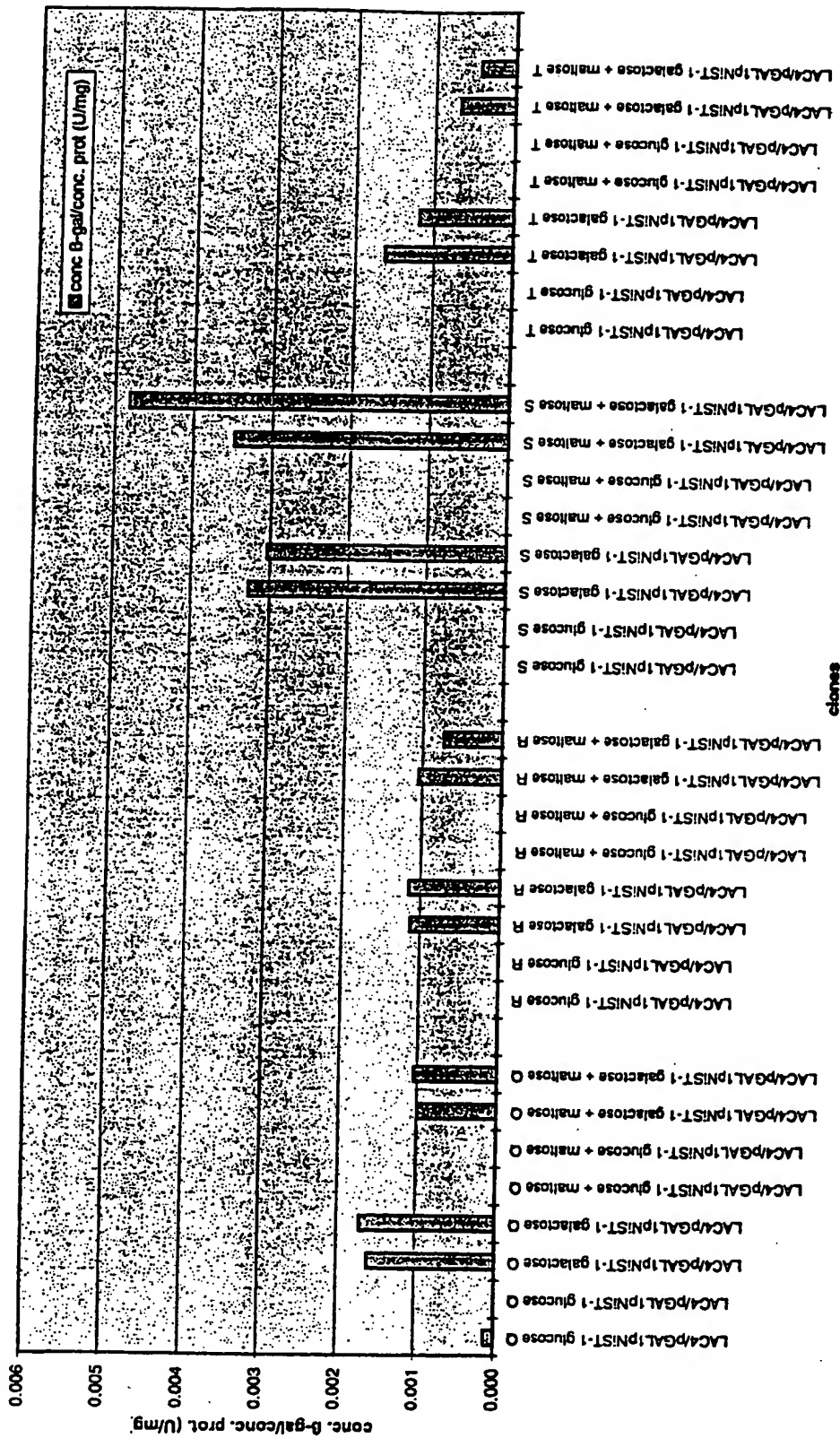
FIG. 3 (CONTINUED)



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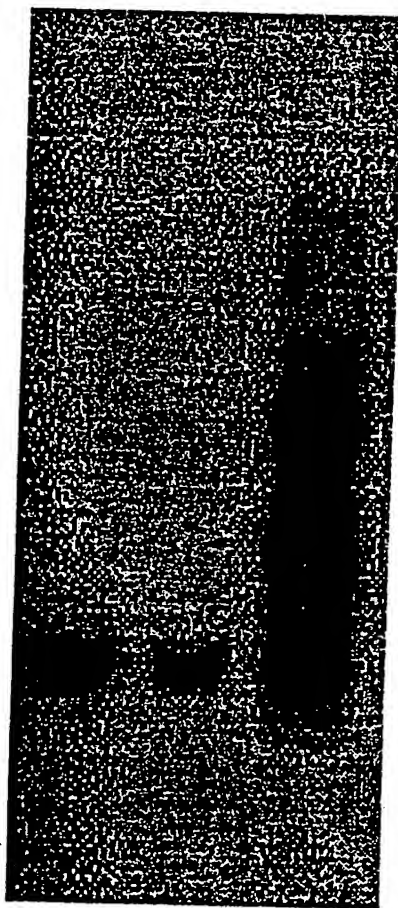
FIG. 4.

B-galactosidase activity GAL1 promoter



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**Figure 5:**



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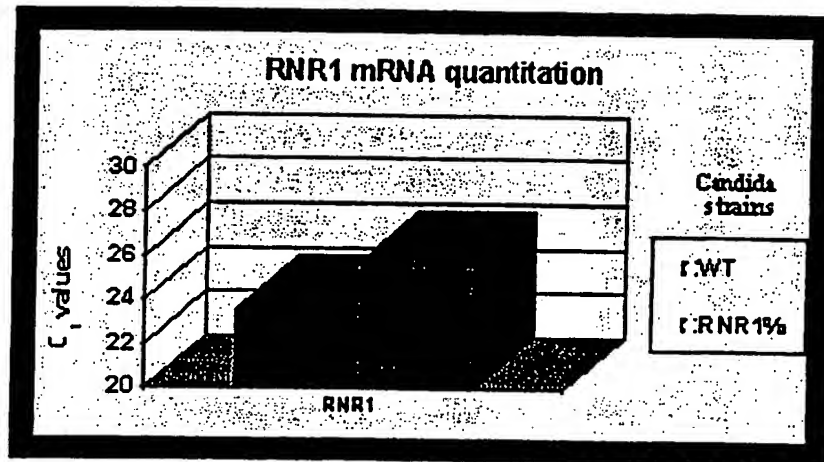
Figure 6A



1: RNF11 mutant  
2: Wild type

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Figure 6B



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FIG. 7

## HindIII

1 AGCTTGAGTA TTCTATAGTG TCACCTAAAT AGCTTGGCGT AATCATGGTC  
TCGAACATCAT AAGATATCAC AGTGGATTTA TCGAACC GCA TTAGTACCAG

51 ATAGCTGTTT CCTGTGTGAA A.TGTATATCC GCTCACAATT CCACACAACA  
TATCGACAAA GGACACACTT TAACAATAGG CGAGTGTTAA GGTGTGTTGT

101 TACGAGCCGG AAGCATAAAG TGTAAGCCT GGGGTGCCTA ATGAGTGAGC  
ATGCTCGGCC TTCGTATTTC ACATTTCGGA CCCCACGGAT TACTCACTCG

151 TAACTCATAT TAATTGCGTT GCGCTCACTG CCCGCTTTC AGTCGGGAAA  
ATTGAGTGTA ATTAACGCAA CGCGAGTGAC GGGCGAAAGG TCAGCCCTTT

201 CCTGTGCTGC CAGCTGCATT AATGAATCGG CCAACGCGCG GGGAGAGCGG  
GGACAGCAGG GTCGACGTAA TTAATTAGCC GGTTCGCGCG CCTCTCCGC

251 GTTTCGCTAT TGGGCGCTCT TCCGCTTCCT CGCTCACTGA CTCGCTGCGC  
CAAAACGCATA ACCCGCGAGA AGGCGAAGGA GCGAGTGACT GAGCGACCGG

301 TCGGTGCTTC GGCTGCGCGG AGCGGTATCA GCTCACTCAA AGGCGGTAAT  
AGCCAGCAAG CCGACGCGCG TCGCCATAGT CGAGTGAGTT TCCGCCATTA

351 ACGGTTATCC ACAGAATCAG GGGATAACGC AGGAAAGAAC ATGTGAGCAA  
TGCCAATAGG TGTCTTAGTC CCTATTGCG TCCTTTCTTG TACACTCGTT

401 AAGGCCAGCA AAAGGCCAGG AACCGTAAAA AGGCGCGGTT GCTGGCGTTT  
TTCCGGTCTG TTTCCGGTCC TTGGCATTTT TCCGGCGCAA CGACCGCAAA

451 TTCCATAGGC TCCGCCCCC TCACGAGCAT CACAAAAATC GACGCTCAAG  
AAGGTATCCG AGGCGGGGGG ACTGCTCGTA GTGTTTITAG CTGCGAGTTC

501 TCAGAGGTGG CGAAACCCGA CAGGACTATA AAGATACCAG GCGTTTCCCC  
AGTCTCCACC GCTTTGGGCT GTCCTGATAT TTCTATGGTC CGCAAAGGGG

551 CTGGAAGCTC CCTCGTGCGC TCTCTGTTT CGACCTTGCC GCTTACCGGA  
GACCTTCGAG GGAGCAGCGG AGAGGACAAG GCTGGGACGG CGAATGGCCT

601 TACCTGTCCG CCTTCTCTCC TTGGGAAGC GTGGCGCTTT CTCATAGCTC  
ATGGACAGGC GGAAAGAGGG AAGCCCTTCG CACCGCGAAA GAGTATCGAG

651 ACGCTGTAGG TATCTCAGTT CCGTGTAGGT CGTTCGCTCC AAGCTGGGCT  
TGCACATCC ATAGAGTCAA GCCACATCCA GCAAGCGAGG TTCGACCGA

## ApaLI

701 GTGTGACGA ACCCCCCGTT CAGCCCGACC GCTGCGCCTT ATCCGGTAAC  
CACACGTGCT TGGGGGGCAA GTCGGGCTGG CGACGCGGAA TAGGCCATTG

751 TATCGTCTTG AGTCCAACCC GGTAAAGACAC GACTTATCGC CACTGGCAGC  
ATAGCAGAAC TCAGGTGGG CCAATCTGTG CTGAATAGCG GTGACCGTCG

801 AGCCACTGGT AACAGGATTA GCAGAGCGAG GTATGTAGGC GGTGCTACAG  
TCGGTGACCA TTGTCTAAT CTTCTCGCTC CATACATCCG CCACGATGTC

851 AGTTCTTGAA GTGGTGGCCT AACTACGGCT AACTAGAAAG GACAGTATTT  
TCAAGAACTT CACCACCGGA TTGATGCCGA TGTATCTTC CTGTCATAAA

901 GGTATCTGCG CTCTGCTGAA GCGAGTTACC TTGGGAAAAA GAGTTGGTAG  
CCATAGACGC GAGACGACTT CCGTCAATGG AAGCCTTTT CTCAACCATC

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## FIG. 7 (CONTINUED)

951 CTCTTGATCC GGCAAACAAA CCACCGCTGG TAGCGGTGGT TTTTGTGTTT  
GAGAACTAGG CCGTTTGTGTT GGTGGCGACC ATCGCCACCA AAAAAACAAA  
.....  
1001 GCAAGCAGCA GATTACGGCG AGAAAAAAG GATCTCAAGA AGATCCTTGG  
CGTTCGTCGT CTAATGCGCG TCTTTTTCCT CTAGAGTTCT TCTAGGAAC  
.....  
1051 ATCTTTTCTA CGGGGTCTGA CGCTCAGTGG AACGAAACT CACGTTAAGG  
TAGAAAAGAT GCCCCAGACT GCGAGTCACC TTGCTTTTGA GTGCAATTCC  
.....  
1101 GATTTTGGTC ATGAGATTAT CAAAAAGGAT CTTACCTAG ATCCTTTTAA  
CTAAAACCAG TACTCTAATA GTTTTTCCTA GAAGTGGATC TAGGAAATT  
.....  
1151 ATTAATAATG AAGTTTAAA TCAATCTAAA GTATATATGA GTAACTTGG  
TAATTTTAC TTCAAAATT AGTTAGATT CATATATACT CATTGAACC  
.....  
1201 TCTGACAGTT ACCAATGCTT AATCAGTGAG GCACCTATCT CAGCGATCTG  
AGACTGTCAA TGGTTACGAA TTAGTCACTC CGTGGATAGA GTCGCTAGAC  
.....  
1251 TCTATTTCGT TCATCCATAG TTGCTGACT CCCGTCGTG TAGATACTA  
AGATAAAGCA AGTAGGTATC AACGGACTGA GGGGCAGCAC ATCTATTGAT  
.....  
1301 CGATACGGGA GGGCTTACCA TCTGGCCCA GTGCTGCAAT GATACCGGA  
GCTATGCCCT CCCGAATGGT AGACCGGGT CACGACGTA CTATGGCGT  
.....  
1351 GACCCACGCT CACCGGCTCC AGATTATCA GCAATAAAC AGCCAGCCGG  
CTGGGTGCGA GTGGCCGAGG TCTAAATAGT CGTTATTGG TCGGTGGCC  
.....  
1401 AAGGGCCGAG CGCAGAAGTG GTCTGCAAC TTTATCCGC TCCATCCAGT  
TTCCCGGCTC GCGTCTTCA CAGGACGTTG AAATAGGCGG AGGTAGGTCA  
.....  
1451 CTATTAATG TTGCCGGGA GCTAGAGTAA GTAGTCCGC AGTTAATAGT  
GATAATTAAC AACGGCCCTT CGATCTCAT CATCAAGCGG TCAATTATCA  
.....  
1501 TTGCGCAACG TTGTTGCCAT TGCTACAGGC ATCGTGGTGT CACGCTCGTC  
AACGCGTTGC AACAACGTA ACGATGTCCG TAGCACCACA GTGCGAGCAG  
.....  
1551 GTTTGGTATG GCTTCATTCA GCTCCGGTTC CCAACGATCA AGGCGAGTTA  
CAAACCATAC CGAAGTAAGT CGAGGCCAAG GGTGCTAGT TCCGCTCAAT  
.....  
1601 CATGATCCCC CATGTTGTGC AAAAAAGCGG TTAGCTCCTT CGGTCTCCG  
GTACTAGGGG GTACAACAG TTTTTCGCC AATCGAGGAA GCCAGGAGGC  
.....  
1651 ATCGTTGTCA GAAGTAAGTT GGCCGCACTG TTATCACTCA TGGTTATGGC  
TAGCAACAGT CTTCAATCAA CCGCGCTCAC AATAGTGAGT ACCAATACCG  
.....  
1701 AGCACTGCAT AATCTCTTA CTGTCATGCC ATCCGTAAGA TGCTTTCTG  
TCGTGACGTA TTAAGAGAA GACAGTACCG TAGGCATTCT ACGAAAAGAC  
.....  
1751 TGA CTGGTGA GACTCAACC AATCATCTT GAGAATAGTG TATCGGCGA  
ACTGACCACT CATGAGTTGG TTCAGTAAGA CTCTTATCAC ATACCGCGCT  
.....  
1801 CCGAGTTGCT CTGCCCCGC GTCAATACGG GATAATACCG CGCCACATAG  
GGCTCAACGA GAACGGGCGG CAGTTATGCC CTATTATGCC GCGGTGTATC  
.....  
1851 CAGAACTTTA AAAGTGCTCA TCATTGGAAA ACGTTCTTCG GGGCGAAAAC  
GTCTTGAAAT TTTCAGAGT AATAACCTTT TGCAAGAAGC CCGCTTTTG  
.....

## FIG. 7. (CONTINUED) 13/63

ApaLI

- 1901 TCTCAAGGAT CTTACCGCTG TTGAGATCCA GTTCGATGTA ACCCACTCGT  
AGAGTTCCCTA GAATGGCGAC AACTCTAGGT CAAGCTACAT TGGGTGAGCA  
.....  
ApaLI  
1951 GCACCCAACT GATCTTCAGC ATCTTTTACT TTCACCAGCG TTCTGGGTG  
CGTGGGTGTA CTAGAAGTCG TAGAAAATGA AAGTGGTCCG AAAGACCCAC  
.....  
2001 AGCAAAAACA GGAAGGCAAA ATGCCGCAAA AAAGGGAATA AGGGCGACAC  
TCGTTTGTGT CCTTCGGTTT TACGGCGTTT TTTCCCTTAT TCCCGCTGTG  
.....  
2051 GGAAATGTTG AATACTCATA CTCTTCCTTT TTCAATATTA TTGAAGCATT  
CCTTTACAAC TTATGAGTAT GAGAAGGAAA AAGTTATAAT AACTTCGTAA  
.....  
2101 TATCAGGGTT ATTGTCTCAT GAGCGGATAC ATATTGGAAT GTATTTAGAA  
ATAGTCCCAA TAACAGAGTA CTCGCCTATG TATAAACTTA CATAAATCTT  
.....  
2151 AAATAAACAA ATAGGGGTTC GCGGCACATT TCCCGGAAAA GTGCCACCTG  
TTTATTGTGT TATCCCAAG GCGCGTGTA AGGGGCTTTT CACGGTGGAC  
.....  
2201 ACGTCTAAGA AACCATTATT ATCATGACAT TAACCTATAA AAATAGGCGT  
TGCAGATTCT TTGGTAATAA TAGTACTGTA ATTGGATATT TTTATCCGCA  
.....  
2251 ATCAGGAGGC CCTTCGTCT GCGCGGTTTC GGTGATGACG GTGAAAACCT  
TAGTGCTCCG GGAAAGCAGA GCGCGCAAAG CCACTACTGC CACTTTTGGA  
.....  
2301 CTGACACATG CAGCTCCCGG AGACGGTCAC AGCTTGCTCT TAAGCGGATG  
GACTGTGTAC GTCGAGGGCC TCTGCCAGTG TCGAACAGAC ATTCCGCTAC  
.....  
2351 CCGGAGCAG ACAAGCCCGT CAGGGCGCGT CAGCGGGTGT TGGCGGGTGT  
GGCCCTCGTC TGTTCCGGCA GTCCCGCCCA GTCCGCCACA ACCGCCACA  
.....

ApaLI

- 2401 CCGGGCTGGC TTAATATGC GGCATCAGAG CAGATTGTAC TGAGAGTGCA  
GCCCCGACCG AATTGATACG CCGTAGTCTC GTCTAACATG ACTCTACGT  
.....  
ApaLI  
2451 CCATATGCGG TGTGAAATAC CGCACAGATG CGTAAGGAGA AAATACCGCA  
GGTATACGCC ACACTTTATG GCGTGTCTAC GCATTCCTCT TTTATGGCGT  
.....  
2501 TCAGGCGAAA TTGTAAACGT TAATATTTTG TTAATAATCG CGTTAAATAT  
AGTCCGCTTT AACATTTGCA ATTATAAAAC AATTTTAAGC GCAATTTATA  
.....  
2551 TTGTTAAATC AGCTCATTTT TTAACCAATA GGCCGAAATC GGCAAAATCC  
AACAATTTAG TCGAGTAAAA AATTGGTTAT CCGGCTTTAG CCGTTTLAGG  
.....  
2601 CTTATAAATC AAAAGAATAG ACCGAGATAG GGTGAGTGT TGTTCAGTT  
GAATATTTAG TTTCTTATC TGGCTCTATC CCAACTCACA ACAAGGTCAA  
.....  
2651 TGAACAAGA GTCCACTATT AAAGAAGGTG GACTCCAACG TCAAAGGGCG  
ACCTTGTTCT CAGGTGATAA TTTCTGCAC CTGAGGTGTC AGTTTCCCGC  
.....  
2701 AAAAACCGTC TATCAGGGCG ATGGCCCACT ACGTGAACCA TCACCCAAAT  
TTTTTGCGAG ATAGTCCCGC TACCGGGTGA TGCATTGGT AGTGGGTTTA  
.....  
2751 CAAGTTTTTT GCGGTGAGG TSCCGTAAAG CTCTAAATCG GAACCCATAA  
GTTCAAAAAA CGCCAGCTCC ACCGCATTC GAGATTTAGC CTTGGGATTT  
.....

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## FIG. 7 (CONTINUED)

2801 GGGAGCCCC GATTTAGAGC TTGACGGGGA AAGCCGGCGA ACGTGGCGAG  
 CCCTCGGGGG CTAAATCTCG AACTGCCCCCT TTCGGCCGCT TGCACCGCTC  
 .....  
 2851 AAAGGAAGGG AAGAAAGCGA AAGGAGCGGG CGCTAGGGCG CTGGCAAGTG  
 TTCTCTCCC TTCTTTCCGT TTCTCGCCC GCGATCCCGC GACCGTTCAC  
 .....  
 2901 TAGCGGTAC GCTGCGCGTA ACCACCACAC CCGCCGCGCT TAATGCGCGG  
 ATCGCCAGTG CGACGCGCAT TGGTGGTGTG GCGCGCGCGA ATTACGCGGC  
 .....  
 2951 CTACAGGGCG CGTCCATTCTG CCATTACGGC TGGCCAACTG TTGGGAAGGG  
 GATGTCCCGC GCAGGTAAGC GGTAAAGTCCG ACGCGTTGAC AACCCCTCCC  
 .....  
 3001 CGATCGGTGC GGGCCTCTTC GCTATTACGC CAGCTGGCGA AAGGGGGATG  
 GCTAGCCACG CCGGAGAAG CGATAATGCG GTCGACCGCT TTCCCCCTAC  
 .....  
 3051 TGCTGCAAGG CGATTAAGTT GGGTAACGCC AGGGTTTTCC CAGTCACGAC  
 ACGACGTTC GCTAATCAA CCCATTGCGG TCCCAAAGG GTCAGTGCTG  
 .....  
 3101 GTTGTAAGG GACGGCCAGT GAATTGTAAT ACGACTCACT ATAGGGCGAA  
 CAACATTTG CTGCCGCTCA CTTAACATTA TGCTGAGTGA TATCCCGCTT  
 .....  
 3151 TTGGTTTTCC AATGATGAGC ACTTTTAAAG TTCTGCTATG TGGCGCGGTA  
 AACCAAAAGG TTAATACTCG TGAATTTTC AAGACGATAC ACCGCGCCAT  
 .....  
 3201 TTATCCCGTG TTGACGCGCG GCAAGAGCAA CTCGGTCGCC GCATACATA  
 AATAGGGCAC AACTGCGGCC GGTCTCGTT GAGCCAGCGG CGTATGTGAT  
 .....  
 3251 TTCTCAGAA GACTTGGTTG AGTACTAATA GGAATTGATT TGGATGGTAT  
 AAGAGTCTTA CTGAACCAAC TCATGATTAT CCTTAATAA ACCTACCATA  
 .....  
 3301 AAACGGAAAC AAAAAAAGA GCTGGTACTA CTTCTTTAA AATTATTTA  
 TTGCTTTTG TTTTCTTCT CGACCATGAT GAAAGAAAT TTAATAAAAT  
 .....  
 3351 TTATTTGATT TTATTTAATA GTATATATTA TATTTGAAC GTAGATTATT  
 AATAAACTAA AATAAATTAT CATATATAAT ATAAACTTG CATCTAATAA  
 .....  
 3401 TTGTTGAAAG TTGCTGTAGT GCCATTGATT CGTAACATA ATTCTGTATT  
 AACAACTTC AACGACATCA CGGTAATAA GCATTGTGAT TAAGACATAA  
 .....  
 3451 AGTCATTCCT CTGTTTGAT AGTATCCAAA AAAACGGCTA TTTTGTGCA  
 TCAAGTAAGGA GAACAACTA TCATAGGTTT TTTGCCGAT AAAAAACGT  
 .....  
 3501<sup>1</sup> ATCTTATTT CTGCATATTA TACAGATAAC ATAATGAAAG AAAAAATCTT  
 TAGAATAAAG GACGTATAAT ATGTCTATTG TATTACTTTC TTTTGTAGAA  
 .....  
 3551 TTTTGTGTT CTTCATGAT GATTTCAACC ATTCTTTTAA ACATTGATCA  
 AAAAAACAA GAAGTTACTA CTAAAGTTG TAAGAAATTT TGTAAGTAGT  
 .....  
 3601 ATTCCTGAGC AACAACCCCA TACACACTGG TTTATATACC GCCCCTTTA  
 TAAGGACTCG TTGTTGGGGT AGTGTGACC AAATATATGG CCGGAAAAT  
 .....  
 3651 CAGTTGAAGA AAGAAATAGA AATAGAAATA GCAAACAAA GATATGACAG  
 GTCAACTTCT TTCTTATCT TATCTTTAT CGTTGTGTTT CTATACTGTC  
 .....  
 3701 TCAACACTAA GACCTATAGT GAGAGAGCAG AAATCATGC CTCACAGTA  
 AGTTGTGATT CTGGATATCA CTCTCTGTC TTTGAGTAGG GAGTGTCTAT  
 .....  
 3751 GCACAGCGAT TATTTGATT AATGGAAGTG AAGAAAACCA ATTTATGTGC  
 CGTGTGCTA ATAAAGCTAA TACCTTGAC TTCTTTGGT TAAATACAG  
 .....



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## FIG. 7. (CONTINUED)

EcoRI

3801 ATCAATTGAC GTTGATACCA CTAAGGAATT CCTTGAATTA ATTGATAAAT  
TAGTTAACTG CAACTATGGT GATTCCTTAA GGAACCTAAT TAACTATTAA  
.....  
3851 TAGGTCCTTA TGTATGCTTA ATCAAGACTC ATATTGATAT AATCAATGAT  
ATCCAGGAAT ACATACGAAT TAGTCTGAG TATAACTATA TTAGTTACTA  
.....  
3901 TTTTCCTATG AATCCACTAT TGAACCATT TTAGAACTTT CACGTAAACA  
AAAAGGATAC TTAGGTGATA ACTTGGTAAT AATCTTGAAA GTGCATTTGT  
.....  
3951 TCAATTTATG ATTTTGAAG ATAGAAAATT TGCTGATATT GGTAATACCG  
AGTTAAATAC TAAAACTTC TATCTTTTAA ACGACTATAA CCATTATGGC  
.....  
4001 TAAAGAAACA ATATATTGGT GGAGTTTATA AAATTAGTAG TTGGGCAGAT  
ATTTCTTTGT TATATAACCA CCTCAAATAT TTTAATCATC AACCCGTCTA  
.....  
4051 ATTACCAATG CTCATGGTGT CACTGGGAAT GGAGTGTTG AAGGATTAAA  
TAATGGTTAC GAGTACCACA GTGACCCTTA CCTCACCAC TTCCTAATTT  
.....  
4101 ACAGGGAGCT AAAGAAACCA CCACCAACCA AGAGCCAAGA GGGTTATTGA  
TGCCCTCGA TTTCTTTGGT GGTGGTTGGT TCTCGTTCT CCCAATAACT  
.....  
4151 TTTAGCTGA ATTATCATCA GTGGGATCAT TAGCATATGG AGAATATTCT  
ACAATCGACT TAATAGTAGT CACCCTAGTA ATCGTATACC TCTTATAAGA  
.....  
4201 CAAAAAAGTG TTGAAATTGC TAAATCCGAT AAGGAATTG TTATTGGATT  
GTTTTTGAC AACTTTAAGC ATTTAGGCTA TTCTTAAAC AATAACCTAA  
.....  
4251 TATTGCCAA CGTGATATGG GTGGCCAAGA AGAAGGATTT GATTGGCTTA  
ATAACGGGT GCACTATACC CACCGTTCT TCTTCTAAA CTAACCGAAT  
.....  
4301 TTATGACACC TGGACTTGG TTAGATGATA AAGGTGATGG ATTAGGACAA  
AATACTGTG ACCTCAACCT AATCTACTAT TTCCACTACC TAATCTGTT  
.....  
4351 CAATATAGAA CTGTTGATGA AGTTGTTAGC ACTGGAAGTG ATATTATCAT  
GTTATATCTT GACAACTACT TCAACAATCG TGACCTGAC TATAATAGTA  
.....  
4401 TGTGGTAGA GGATTGTTG GTAAAGGAAG AGATCCAGAT ATTGAAGTA  
ACAACCATCT CCTAACAAAC CATTTCTTC TCTAGGTCTA TAACCTCCAT  
.....  
4451 AAAGGTATAG AAATGCTGGT TGAATGCTT ATTTGAAAAA GACTGGCCAA  
TTCCATATC TTTACGACCA ACCTTACGAA TAAACTTTTT CTGACCGTT  
.....  
4501 TTATAAATGT GAAGGGGAG ATTTTCACTT TATTAGATTT GTATATATGT  
AATATTTACA CTTCCTCTC TAAAAGTGAA ATAATCTAAA CATATATACA  
.....  
4551 AGAATAAATA AATAAATAAG TAAATAAAT AATTAAATAA GGGTGGTAAT  
TCTTATTTAT TTATTTATC AATTATTTA TTAATTTATT CCCACCATT  
.....  
4601 TATTACTATT TACAATCAA GTTGGTCTT CTAGCTGTAA TCCGGGCAGC  
ATAATGATAA ATGTTAGTTT CCACCAGGAA GATCGACATT AGGCCGCTG  
.....  
4651 GCAACGGAAC ATTCATCAGT GTAAAAATGG AATCAATAAA GCCCTGCCA  
CGTTGCCTTG TAAGTAGTCA CATTTTACC TTAGTTATTT CGGGACCGCT  
.....  
4701 GCGCGCAGGG TCAGCCTGAA TAGCGTTTA ATGACCAGCA CAGTCGTGAT  
CGCGCTCCC AGTCGACTT ATGCGCAAAT TACTGGTCGT GTCAGCACTA  
.....

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## FIG. 7 (CONTINUED)

4751 GGCAAGGTCA GAATAGCCCA AGTCGGCCGA GGGGCTGTA CAGTGAGGA  
CCGTTCCAGT CTTATCGGGT TCAGCCGGCT CCCCAGACAT GTCACCTCT  
.....

4801 AGATCTGATA TTGACGAAGA GGAACCAATG TAACGTTACA CTGAAGAAA  
TCTAGACTAT AACTGCTTCT CTTGGTTAC ATTGCAATGT GACTTCTTT  
.....

4851 CACACAATAA ACGGGAAGAA ACGGTGTAAA AGTGTGAAAA TAATTTTGA  
GTGTGTATT TGCCCTTCTT TGCCACATTT TCACACTTTT ATTAAAACT  
.....

4901 ATATCATTTT CTTGGTTTA ATTCCAAACG AAACGTGTTT TTTTATAGA  
TATAGTAAAG GGAACCAAT TAAGGTTTG TTTGCACAAA AAAATCTCT  
.....

EcoRI  
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4951 ATGGGAATTC TTATTGGATG TCTAGATTGT TGTCTTACTC CAGACTGTGC  
TACCCTTAAG AATAACCTAC AGATCTAACA AACAAATGAG GTCTGACACG  
.....

ApaLI  
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5001 ACAAAAACGT TTGGATGGAT GATCAGAAGA TATTTTATAG CTTAGCTCTA  
TGTTTTGGCA AACCTACCTA CTAGTCTTCT ATAAAAATCC GAATCGAGAT  
.....

5051 AATATAAGAA ATGATGCTTG AAAAACCAGA CAGAAATGA GTTCAAAAA  
TTATATTCTT TACTACGAAC TTTTGGTCT GTCTTTAACT CAAAGTTTT  
.....

5101 TTGGTAATGT GAGGTATTAG TCAACTAAC AAATAACAAT GCAAACGGT  
AACCATTACA TCCATAATC AGTTGATTGG TTTATTGTTA CGTTTGCCA  
.....

5151 TGATACATTT CATTTTGAAA ATAATGAAC TGGAATTGGA TGACCAGCAC  
ACTATGTAAA GTAAAACCTT TATTACTTTG ACCTTAACCT ACTGGTCGTG  
.....

5201 ACAACACAT AAAGTAATTA TGGGAATTAG AACCGAAT AGAGGAGTAC  
TGTTTGTA TTTCAATTAAT ACCCTTAATC TCGCTTGTA TCTCTCATG  
.....

5251 TTGGCCACGA ACAGAATACA AGTGGGAACA CTATTTTCTC CATTTGTTTA  
AACCGGTGCT TGTCTTATGT TCACCCTTGT GATAAAGAG GTAACAAAAT  
.....

5301 GTTCTGTTTT TTTGTCAGCC TAGTTTGTG CTATGTGTAA AAAATATTGC  
CAAGACAAA AACAGTCGG ATCAAAACAC GATACACATT TTTTATAACG  
.....

HindIII  
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5351 CAAGAAAAA AGCTTGTTTT GTGGCCAGTG TCCGAAAAA ATTTTGGGA  
GTTCTTTTTT TCGAACAAA CACCGGTCAC AGGCTTTTTT TAAAACCCCT  
.....

5401 ATCTTCGGAT TAATTTATGT TTTCAATCCA TCGGGGAAAG TGGGGGGAA  
TAGAAGCCTA ATTAAATACA AAGTAAGGT AGCCCTTTC ACCCCCTT  
.....

5451 AAAATTTTAA GCAGTTCACA AAACCTTCCA AAAATATAT GGACAAGAT  
TTTTAAAT COTCAAGTG TTTGGAAGT TTTTATATA CCTGTTCTA  
.....

5501 GATTGTATTT TCCGACACC AAATCATAA TTAATTATGA GAAAGTTAA  
CTAACATAA AGGGCTGTGG TTTAGTATT AATTAATACT CTTCAATTT  
.....

5551 TGTAACGTTA CAATTTATGT TATTTGAAG GTGAAAAGCG ATTTATGAT  
ACATTGCAAT GTTAAATACA AATAAACTTC CACTTTTCG TAAATACTAA  
.....

5601 TTTCCGAAAT GAAAATTTTT TTTAGGTTTA TTTTTTTGT CGGGCAAAGA  
AAAGGCTTTA CTTTTAAAAA AATCCAAAT AAAAAAACA GCCCGTTCT  
.....

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FIG. 7. (CONTINUED)

Ec RI

5651 AAAACTGAAC AAGGATTAT AAAATTTTGG GTGTTTGTGT GTGTCTGGAG  
TTTGTACTTG TTCCTAATAA TTTTAAAAAC CACAAACAAA CACAGACCTC

EcoRI

5701 AATTCATTCC TCTCTCATCT TCACACAATG TTTAGACATC TGACACGATT  
TTAAGTAAGG AGAGAGTAGA AGTGTGTTAC AATCTGTAG ACTGTGCTAA

5751 CATGATAGTT CGGTTTCCGG GGTGGTGTGT TAGTTTTCGT TTTCTTTTT  
GTACTATCAA GCCAAAGGCC CCAACCACAA ATCAAAAGCA AAAAGAAAA

5801 TTTTGGAAAG AATGTTTGTG CTCATTGGTT TTCTTCTTC ATTCAATAGT  
AAAACCTTTC TTACAAAATC GAGTAACCA AAGAAAGAAG TAAGTTATCA

5851 TTTGAAAGAA TTGCCCACCT TGTTATTACA ATCATATAAA ATTAACTTT  
AAACTTTCTT AAACGGGTGA ACAATAATGT TAGTATATTT TAATTGAAA

5901 GATATAAAAT AGAGTTTGAA AGTTTCCAG ATCTTTTTTG ATTTCTTTGT  
CTATATTTTA TCTCAAACTT TCAAGGGTC TAGGAAAAAC TAAAGAAACA

5951 AAATTTTTTT TTCTCCACA TATACACACA TACAAACCGA TTTTATAAG  
TTTAAAAAAA AAGAGGGTGT ATATGTGTGT ATGTTTGGCT AAAAATATTC

PstI

AvaI

BamHI

6001 AAAGAGTTAT ACCCTGCAGC TCGACCTCGA GGGATCCGGG CCCTCTAGAT  
TTCTCAATA TGGGACGTCG AGCTGGAGCT CCCTAGGCC CCGAGATCTA

AvaI

6051 GCGGCCGCTA GGCCTCGAGG GACTTTTGCA CAAAAATAA TTTATTTTCC  
CGCCGGCGAT CCGGAGCTCC CTGAAAACGT GGTTTTATT AAATAAAGG

6101 AAAATAAAAT TAAATAAAT AAAATAACT CATAATTAA TAAAAATTC  
TTTTATTTA AATTTATTA TTTTATTGA GTATTAAAT ATTTTAAAG

6151 AAAATCTTCT AGTGTCTTT CATATGCAGT ACATTAGCCA TCAGTCACTT  
TTTTAGAAGA TCACAGGAA GTATACGTCA TGTAATCGGT AGTCAGTGAA

6201 AAACAGCATC TGCTGGTTGA AGAATGCTTG AAGCAATTGT CCAGTCCCAG  
TTTGTCTAG ACGACCACT TCTTACGAAC TTCGTTAACA GGTCAAGGTC

6251 AGGCACAGGC TAGGAGATCT TCAGTTTCGG AGGTAACCTG TAAGTCTGTT  
TCCGTGTCCG ATCTCTAGA AGTCAAAGCC TCCATTGGAC ATTCAGACAA

6301 AATGAAGTAA AAGTTCCTTA GGATTTCCAC TCTGACTATG GTCCAGGCAC  
TTACTTCATT TTCAAGGAAT CCTAAAGGTG AGACTGATAC CAGGTCCGTG

6351 AGTGACTGTA CTCCTGGCC TTCAGGTAAT GCAGAATCCT CCCATAATAT  
TCACTGACAT GAGGAACCGG AGTCCATTA CGTCTTAGGA GGGTATTATA

6401 CTTTTCAGGT GCAGACTGCT CATGAGTTT CCCCTGGTGA AATCTTCTT  
GAAAAGTCCA CGTCTGACGA GTACTCAAAA GGGGACCACT TTAGAAGAAA

6451 CTCCAGTTTT TCTTCCAGGA CTGTCTTCAG ATGGTTTATC TGATGATAGA  
GAGGTCAAAA AGAAGGTCTT GACAGAAATC TACCAATAG ACTACTATCT

6501 CATTAGCCAG GAGGTTCTCA ACAATAGTCT CATTCAGCC AGTGCTAGAT  
GTAATCGGTC CTCCAAGAGT TGTATCAGA GTAAGGTCG TCAOGATCTA

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## FIG. 7. (CONTINUED)

6551 GAATCTTGTC TGAAAATAGC AAAGATGTTT TGGAGCATCT CATAGATGGT  
CTTAGAACAG ACTTTTATCG TTTCTACAAG ACCTCGTAGA GTATCTACCA

PstI

6601 CAATGCGGCG TCCTCCTTCG GGAAGTGTG CAGCTGCTTA ATCTCCTCAG  
GTTACGCCGC AGGAGGAAGA CCTTGACGAC GTCGACGAAT TAGAGGAGTC

6651 GGATGTCAAA GTTCATCCTG TCCTTGAGGC AGTATTCAAG CCTCCCATTC  
CCTACAGTTT CAAGTAGGAC AGGAAGTCCG TCATAAGTTC GGAGGGTAAG

6701 AATTGCCACA GGAGCTTCTG AACTGAAAA TTGCTGCTTC TTTGTAGGAA  
TTAACGGTGT CCTCGAAGAC TGTGACTTTT AACGACGAAG AACATCCTT

6751 TCCAAGCAAG TTGTAGCTCA TGGAAAGAGC TGTAAGTGGAG AAGCACAACA  
AGGTTTCGTC AACATCGAGT ACCTTTCTCG ACATCACCTC TTCGTGTTGT

AvaI

6801 GGAGAGCAAT TTGGAGGAGA CACTTGTTGG TCATGTTCTT CGAGGCCTTT  
CCTCTCGTTA AACCTCCTCT GTGAACAACC AGTACAAGGA GCTCGGAAA

BamHI

6851 TTGGCCAGCT GCGGCTGCT GCGCGACGGC GAGCTGCTCA CCACCCAGGA  
AACCGTCTGA CCGCGGACGA CCGGCTGCCG CTCGACGAGT GGTGGGTCTT

BamHI

6901 TCCGTCCCCC TTTTCCTTTG TCGATATCAT GTAATTAGTT ATGTCACGCT  
AGGCAGGGGG AAAAGGAAAC AGCTATAGTA CATTAAATCAA TACAGTGCGA

6951 TACATTACAG CCTCCCCC ACATCCGCTC TAACCGAAAA GGAAGGAGTT  
ATGTAAGTGC GCGAGGGGGG TGTAGGCGAG ATTGGCTTTT CCTTCCTCAA

7001 AGACAACCTG AAGTCTAGG CCTATTAT TTTTTATAG TTATGTTAGT  
TCTGTTGGAC TTCAGATCCA GGGATAAATA AAAAAATATC AATACAATCA

7051 ATTAAGAACG TTATTATAT TTCAAATTTT TCTTTTTTTT CTGTACAGAC  
TAATTCCTGC AATAAATATA AAGTTTAAAA AGAAAAAATA GACATGCTCG

7101 GCGGTGACGC ATGTAACATT AACTGAAAA CCTTGCTTGA GAAGGTTTTG  
CGCACATGCG TACATTGTAA TATGACTTTT GGAACGAAGT CTTCCAAAAC

HindIII

7151 GGACGCTCGA AGGCTTTAAT TTGCA  
CCTGCGAGCT TCCGAAATTA AACGT

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FIG. 8.

1 TTCCATCGGG GAAAGTGGGG GGGAAAAAT TTAAAGCAGT TCACAAAACC  
AAGGTAGCCC CTTTCACCCC CCCTTTTTTA AAATTCGTCA AGTGTTTTGG  
.....  
51 TTCAAAAAA TATATGGACA AAGATGATTG TATTTTCCCG ACACCAAAAT  
AAGGTTTTTT ATATACCTGT TTCTACTAAC ATAAAAGGGC TGTGGTTTAA  
.....  
101 CATAATTAAT TATGAGAAAG TTAAATGTAA CGTTACAATT TATGTTTATT  
GTATTAATTA ATACTCTTTC AATTACATT GCAATGTAA ATACAAATAA  
.....  
151 TGAAGGTGAA AAGCGATTGA TGATTTTTC GAAATGAAA TTTTITTTAG  
ACTTCCACTT TTCGCTAAAT ACTAAAAGG CTTACTTTT AAAAAAATC  
.....  
201 GTTATTTTT TTGTGCGGC AAAGAAAAAC TGAACAAGGA TTATTAAAT  
CAAATAAAA AACAGCCCG TTCTTTTGT ACTGTTCCT AATAATTTA  
.....

EcoRI  
-----

251 TTTTGGTGT TGTGTGTGTC TGGAGAATTC ATTCTCTCT CATCTTCACA  
AAAACCACAA ACAACACAG ACCTCTTAAG TAAGGAGAGA GTAGAAGTGT  
.....  
301 CAATGTTTAG ACATCTGACA CGATTCATGA TAGTTCGGTT TCCGGGGTTG  
GTTACAAATC TGTAGACTGT GCTAAGTACT ATCAAGCCAA AGGCCCAAC  
.....  
351 GTGTTAGTT TTCGTTTTTC TTTTITTTTG GAAAGAATGT TTAGCTCAT  
CACAAATCAA AAGCAAAAAG AAAAAAAC CTTTCTTACA AAATCGAGTA  
.....  
401 TGGTTTTCTT TCTTCATTCA ATAGTTTGA AAGAATTTGC CCACTTGTTA  
ACCAAAAGAA AGAAGTAAGT TATCAAACT TTCTTAAACG GGTGAACAT  
.....  
451 TTACAATCAT ATAAAATTAA ACTTTGATAT AAAATAGAGT TTGAAAGTTT  
AATGTTAGTA TATTTTAATT TGAACTATA TTTTATCTCA AACTTTCAAA  
.....  
501 CCCAGATCCT TTTGATTTC TTGTAAATT TTTTITTC TCACATATAC  
GGGTCTAGGA AAACTAAAG AACATTTAA AAAAAAGAG GGTGTATATG  
.....

PstI  
-----

551 ACACATACAA ACCGATTTTT ATAAGAAAGA GTTATACCCT GCAGCTCGAC  
TGTGTATGTT TGGCTAAAAA TATCTTTCT CAATATGGGA CGTCGAGCTG  
.....

PstI  
-----

HindIII  
-----

AvaI  
-----

601 CTCGACTGTT TAAACCTGCA GGCATGCAAG CTTGGCCAAA AAGGCCTOGA  
GAGCTGACAA ATTTGGACGT CCGTACGTT GAACCGGTT TTCCGGAGCT  
.....

AvaI  
-----

651 GGAACATGAC CAACAAGTGT CTCCTCCAAA TTGCTCTCCT GTTGTGCTTC  
CCTTGACTG GTTGTTCACA GAGGAGGTTT AACGAGAGGA CAACACGAAG  
.....  
701 TCCACTACAG CTCTTCCAT GAGCTACAAC TTGCTTGGAT TCCTACAAAG  
AGGTGATGTC GAGAAAGGTA CTCGATGTTG AACGAACCTA AGGATGTTTC  
.....  
751 AAGCAGCAAT TTTCAGTGC AGAAGCTCCT GTGGCAATTG AATGGGAGGC  
TTCGTCTTA AAGTACAG TCTTCGAGGA CACCGTTAAT TTACCCTCCG  
.....  
801 TTGAATACTG CCTCAAGGAC AGGATGAACT TTGACATCCC TGAGGAGATT  
AATTATGAC GGAGTTCCTG TCTACTTGA AACTGTAGGG ACTCCTCTAA  
.....

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FIG. 8. (CONTINUED)

PstI

851 AAGCAGCTGC AGCAGTTCCA GAAGGAGGAC GCCGCATTGA CCATCTATGA  
 TTCGTCGACG TCGTCAAGGT CTCCTCCTG CGGCGTAACT GGTAGATACT  
 .....  
 901 GATGCTCCAG AACATCTTTG CTATTTTCAG ACAAGATTCA TCTAGCACTG  
 CTACGAGGTC TTGTAGAAAC GATAAAAGTC TGTCTAAGT AGATCGTGAC  
 .....  
 951 GCTGGAATGA GACTATTGTT GAGAACCTCC TGGCTAATGT CTATCATCAG  
 CGACCTTACT CTGATAACAA CTCCTGGAGG ACCGATTACA GATAGTAGTC  
 .....  
 1001 ATAAACCATC TGAAGACAGT CCGGAAGAA AACTGGAGA AAGAAGATTT  
 TATTTGGTAG ACTTCTGTCA GGACCTTCTT TTTGACCTCT TTCTCTAA  
 .....  
 1051 CACCAGGGGA AACTCATGA GCAGTCTGCA CCTGAAAAGA TATTATGGGA  
 GTGGTCCCTT TTGAGTACT CGTCAGAGT GGACTTTTCT ATAATACCCT  
 .....  
 1101 GGATTCTGCA TTACCTGAAG GCCAAGGAGT ACAGTCACTG TGCCTGGACC  
 CCTAAGACGT AATGGACTTC CGGTTCTCTCA TGTCAGTGAC ACGGACCTGG  
 .....  
 1151 ATAGTCAGAG TGGAAATCCT AAGGAACCTT TACTTCATTA ACAGACTEAC  
 TATCAGTCTC ACCTTTAGGA TTCCTTGAAA ATGAAGTAAT TGTCTGAATG  
 .....  
 1201 AGGTTACCTC CGAAACTGAA GATCTCCTAG CCTGTGCTC TGGGACTGGA  
 TCCAATGGAG GCTTTGACTT CTAGAGGATC GGACACGGAG ACCCTGACCT  
 .....  
 1251 CAATTGCTTC AACCATTCTT CAACCAGCAG ATGCTGTTTA AGTGACTGAT  
 GTTAACGAAG TTCGTAAGAA GTTGGTCGTC TACGACAAAT TCACTGACTA  
 .....  
 1301 GGCTAATGTA CTGCATATGA AAGGACACTA GAAGATTTTG AAATTTTAT  
 CCGATTACAT GACGTATACT TTCTGTGAT CTCTAAAC TTAAAAATA  
 .....  
 1351 TAAATTATGA GTTATTTTA TTTATTTAA TTTTATTTG GAAAATAAT  
 ATTTAATACT CAATAAAAT AAATAAATT AAAATAAAC CTTTTATTA  
 .....

XmaI

SmaI

BamHI

AvaI

AvaI

1401 TATTTTGGT GCAAAAGTCC CTCGAGGCCT AGCGGCCGCC TAGAGGATCC  
 ATAAAAACCA CGTTTTAGG GAGCTCCGA TCGCCGGCGG ATCTCCTAGG  
 .....

XmaI

SmaI

AvaI

1451 CCGGGCGCTA GGCGCCGCT AGGCTTTTT GGCCAAGCTC GAATTTGAG  
 GGCCCGCGAT CCGCCGGCGA TCCGAAAAA CCGTTTCGAG CTAAAGCTC  
 .....

XmaI

SmaI

EcoRI

AvaI

ClaI

1501 GAATTCGAGC TCGGTACCCG GGGGATCGAT CCGTCCCCCT TTCTTTGT  
 CTTAAGCTCG AGCCATGGGC CCCCTAGCTA GCCAGGGGA AAAGGAAACA  
 .....

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FIG. 8. (CONTINUED)

- 1551 CGATATCATG TAATTAGTTA TGTCACGCTT ACATTACGGC CCTCCCCCA  
GCTATAGTAC ATTAATCAAT ACAGTGGAA TGTAAGTGGC GGAGGGGGT
- 1601 CATCCGCTCT AACCGAAAAG GAAGGAGTTA GACAACCTGA AGTCTAGGTC  
GTAGGCGAGA TTGGCTTTTC CTCCTCAAT CTGTTGGACT TCAGATCCAG
- 1651 CCTATTTATT TTTTATAGT TATGTTAGTA TTAAGAAGCT TATTATATT  
GGATAAATAA AAAAATATCA ATACAATCAT AATTCTTGCA ATAAATATA
- 1701 TCAAATTTTT CTTTTTTTC TGACAGACG CGTGTACGCA TGTAACATTA  
AGTTTAAAAA GAAAAAAG ACATGTCTGC GCACATGCGT ACATTGTAAT
- 1751 TACTGAAAAC CTGCTTGAG AAGGTTTGG GACGCTCGAA GGCTTTAAT  
ATGACTTTG GAACGAACTC TCCAAAACC CTGCGAGCTT CCGAAATTAA
- 1801 TGCAAGCTAG CTGGCGTAA TCATGGTCAT AGCTGTTTC TGTTGAAAT  
ACGTTCTGATC GAACCGCATT AGTACCACTA TCGACAAAGG ACACACTTA
- 1851 TGTATCCGC TCACAATTCC ACACAACATA CGAGCCGGAA GCATAAAGTG  
ACAATAGGCG AGTGTTAAGG TGTGTTGAT GCTCGGCTT CGTATTTAC
- 1901 TAAAGCCTGG GGTGCCTAAT GAGTGAGCTA ACTCACATTA ATTGCGTTGC  
ATTTCGGACC CCACGGATTA CTCACCTGAT TGAGTGTAAT TAACGCAACG
- 1951 GCTCACTGCC CGCTTTCCAG TCGGAAACC TGTCGTGCCA GAGATCTCTG  
CGAGTGACGG GCGAAAGGTC AGCCCTTGG ACAGCAGGT CTCTAGAGAC
- 2001 CATTAAATGAA TCGGCCAAGC CGCGGGGAGA GGCGGTTTC GTATTGGGG  
GTAATTACTT AGCCGGTTGC GCGCCCTCT CCGCCAAAGC CATAACCGC
- 2051 CTCTCCGCT TCCTCGCTCA CTGACTCGCT GCGCTCGGT GTTCGGCTGC  
GAGAAGGCGA AGGAGCGAGT GACTGAGCGA CGCGAGCCAG CAAGCCGAGC

Clai

- 2101 GCGAGCGGT ATCAGATCGA TCTCACTCAA AGGCGGTAAT ACGGTTATCC  
CCGCTCGCCA TAGTCTAGCT AGAGTGAGTT TCCGCCATTA TGCCAATAGC
- 2151 ACAGAATCAG GGGATAACGC AGGAAAGAAC ATGTGAGCAA AAGGCCAGCA  
TGTCTTAGTC CCTATTGCG TCTTTCTTG TACACTCGTT TTCCGGTGT
- 2201 AAAGGCCAGG AACCGTAAA AGGCCGCGTT GCTGGCGTTT TTCCATAGGC  
TTTCCGGTCC TTGGCATTTT TCCGGCGCAA CGACCGCAA AAGGTATCCG
- 2251 TCCGCCCCC TGACGAGCAT CAAAAAATC GACGCTCAAG TCAGAGGTGG  
AGGCGGGGG ACTGCTCGTA GTGTTTTAG CTGCGAGTTC AGTCTCCACC
- 2301 CGAAACCCGA CAGGACTATA AGATACCAG GCGTTTCCCC CTGGAAGCTC  
GCTTTGGGCT GTCTGATAT TCTATGGTC CGCAAAGGGG GACCTTCGAG
- 2351 CCTCGTGCGC TCTCTGTC SSACCTGCC GCTTACCGGA TACCTGTCCG  
GGAGCACCGG AGAGGACAAG TGTGGGACCG CGAATGGCCT ATGGACAGC
- 2401 CCTTTCTCCC TTGGGAAGC TTGGCGTTT CTCATAGCTC ACGCTGTAGG  
GGAAAGAGGG AAGCCCTTCG TACCGGAAA GAGTATCGAG TGGACATCC

ApaLI

- 2451 TATCTCAGTT CGGTGAGGT CTTCCGCTCC AAGCTGGGCT GTGTGCACGA  
ATAGAGTCAA GCCACATCCA TCAAGCGAGG TTCGACCCGA CACACGTGCT

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FIG. 8. (CONTINUED)

2501 ACCCCCCGTT CAGCCCGACC GCTGCGCCTT ATCCGGTAAC TATCGTCTTG  
TGGGGGGCAA GTCGGGCTGG CGACCGGAA TAGGCCATTG ATAGCAGAAC  
.....  
2551 AGTCCAACCC GGTAAACAC GACTTATCG CACTGGCAGC AGCCACTGGT  
TCAGGTTGGG CCATTCTGTG CTGAATAGCG GTGACCGTCG TCGGTGACCA  
.....  
2601 AACAGGATTA GCAGAGCGAG GTATGTAGGC GGTGCTACAG AGTTCTTGAA  
TTGTCCTAAT CGTCTCGCTC CATACTCCG CCACGATGTC TCAAGAACTT  
.....  
2651 GTGGTGGCCT AACTACGGCT AACTAGAAG GACAGTATTT GGTATCTGGG  
CACCACCGGA TTGATGCGA TGTGATCTTC CTGTATAAA CCATAGACCG  
.....  
2701 CTCTGCTGAA GCCAGTTACC TTCGAAAAA GAGTTGGTAG CTCTTGATCC  
GAGACGACTT CGGTCAATGG AAGCCTTTT CTCAACCATC GAGAACTAGG  
.....  
2751 GGCAAAACAA CCACCGCTGG TAGCGGTGGT TTTTGTGTT GCAAGCAGCA  
CCGTTGTGTT GGTGGCGACC ATCGCCACCA AAAAAACAA CGTTCGTGT  
.....  
2801 GATTACGGC AGAAAAAAG GATCTCAAGA AGATCCTTTG ATCTTTTCTA  
CTAATGCGCG TCTTTTTTTC CTAGAGTCT TCTAGGAAAC TAGAAAAGAT  
.....  
2851 CGGGGTCTGA CGCTCAGTG AACGAAACT CACGTTAAGG GATTTTGGTC  
GCCCCAGACT GCGAGTCACC TTGCTTTTGA GTGCAATTCC CTAACCAG  
.....  
2901 ATGAGATTAT CAAAAGGAT CTTACCTAG ATCCTTTTAA ATTAAAAATG  
TACTCTAATA GTTTTTCTA GAAGTGGATC TAGGAAATTA TAATTTTAC  
.....  
2951 AAGTTTAA TCAATCTAA GTATATATGA GTAACTTGG TCTGACAGTT  
TTCAAAATTT AGTTAGATTT CATATATACT CATTGAACC AGACTGTCAA  
.....  
3001 ACCAATGCTT AATCAGTGAG GCACCTATCT CAGCGATCTG TCTATTTGCT  
TGGTTACGAA TTAGTCACTC CGTGGATAGA GTCGCTAGAC AGATAAAGCA  
.....  
3051 TCATCCATAG TTGCTGACT CCCCCTCGTG TAGATAACTA CGATACGGGA  
AGTAGGTATC AACGACTGA GGGCAGCAC ATCTATTGAT GCTATGCCCT  
.....  
3101 GGGCTTACCA TCTGGCCCA GTGCTGCAAT GATACCGGA GACCCAGCT  
CCCGAATGGT AGACCGGGT CACGACGTTA CTATGGCGCT CTGGGTGCGA  
.....  
3151 CACCGGCTCC AGATTTATCA GCAATAAACC AGCCAGCCGG AAGGGCCGAG  
GTGGCCGAGG TCTAAATAGT CGTTATTGTTG TCGGTGGCC TTCCCGGCTC  
.....  
3201 CGCAGAAGTG GTCCTGCAAC TTTATCGCC TCCATCCAGT CTATTAATTG  
CGGTCTTCAC CAGGACGTTG AAATAGGCGG AGGTAGGTCA GATAATTAAC  
.....  
3251 TTGCCGGAA GCTAGAGTAA GTAGTTCGCC AGTTAATAGT TTGCGCAACG  
AACGGCCCTT CGATCTCAT CATCAAGCGG TCAATTATCA AACGGTTGC  
.....  
3301 TTGTTGCCAT TGCTACAGG ATCGTGGTGT CACGCTCGTC GTTGGTATG  
AACAAACGTA ACGATGTCCG TAGCACCACA GTGCGAGCAG CAAACCATAC  
.....  
3351 GCTTCATTCA GCTCCGGTTC CCAACGATCA AGGCGAGTTA CATGATCCC  
CGAAGTAAGT CGAGCCCAAG GGTGCTAGT TCCGCTCAAT GTACTAGGGG  
.....  
3401 CATGTTGTGC AAAAAAGCG TTAGCTCCTT CGGTCTCCG ATCGTTGTCA  
GTACAACAG TTTTTCGCC AATCGAGGAA GCCAGGAGG TAGCAACAGT  
.....  
3451 GAAGTAAGTT GGCCGCACTG TTATCACTCA TGGTTATGGC AGCACTGCAT  
CTTCATTCAA CCGCGTCAC AATAGTGAGT ACCAATACCG TCGTGACGTA  
.....



*FIG. 8. (CONTINUED) 23/63*

3501 AATTCTCTTA CTGTCATGCC ATCCGTAAGA TGCTTTTCTG TGACTGGTGA  
TTAAGAGAAT GACAGTACCG TAGGCATTCT ACGAAAAGAC ACTGACCACT  
.....  
3551 GTACTCAACC AAGTCATTCT GAGAATAGTG TATGCGGCGA CCGAGTTGCT  
CATGAGTTGG TTCAGTAAGA CTCTTATCAC ATACGCCGCT GGCTCAACGA  
.....  
3601 CTTGCCCGGC GTCAATACGG GATAATACCG CGCCACATAG CAGAACTTTA  
GAACGGGCGC CAGTTATGCC CTATTATGGC GCGGTGTATC GTCTTGAAAT  
.....  
3651 AAAGTGCTCA TCATTGAAA ACGTCTTCTG GGGCGAAAAC TCTCAAGGAT  
TTTCACGAGT AGTAACCTTT TGCAAGAAGC CCCGCTTTTG AGAGTTCCTA  
.....

ApaLI  
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3701 CTTACCGCTG TTGAGATCCA GTTCGATGTA ACCCACTCGT GCACCCAACT  
GAATGGCGAC AACTCTAGGT CAAGCTACAT TGGGTGAGCA CGTGGGTGA  
.....  
3751 GATCTTCAGC ATCTTTTACT TTCACCAGCG TTTCTGGGTG AGCAAAAACA  
CTAGAAGTCG TAGAAAATGA AAGTGGTCCG AAAGACCCAC TCGTTTTTGT  
.....  
3801 GGAAGGCAAA ATGCCGCAAA AAAGGGAATA AGGGCGACAC GGAAATGTTG  
CCTTCCGTTT TACGGCGTTT TTCCCTTAT TCCGCTGTG CCTTTACAAC  
.....  
3851 AATACTCATA CTCTTCCTTT TTCAATATTA TTGAAGCATT TATCAGGGTT  
TTATGAGTAT GAGAAGGAAA AAGTTATAAT AACTTCGTAA ATAGTCCCAA  
.....  
3901 ATTGTCTCAT GAGCGGATAC ATATTGTAAT GTATTTAGAA AAATAAACAA  
TAACAGAGTA CTCGCCTATG TATAAACTTA CATAAATCTT TTTATTGTT  
.....  
3951 ATAGGGGTTT CGCGCACATT TCCCCGAAAA GTGCCACCTG ACGTCTAAGA  
TATCCCCAAG GCGCGTGTA AGGGGCTTTT CACGGTGGAC TGCAGATTCT  
.....  
4001 AACCATTATT ATCATGACAT TAACCTATAA AAATAGGCGT ATCAGGAGGC  
TTGGTAATAA TAGTACTGTA ATTGGATATT TTTATCCGCA TAGTGCTCCG  
.....  
4051 CCTTTCGTCT CGCGCGTTT CCGTATGACG GTGAAAACCT CTGACACATG  
GGAAAGCAGA GCGCGCAAAG CCACTACTGC CACTTTTGGA GACTGTGTAC  
.....  
4101 CAGCTCCCGG AGACGGTCAC AGCTTGCTG TAAGCGGATG CCGGGAGCAG  
GTGAGGGGCC TGTGCCAGTG TCGAACAGAC ATTGCCTAC GGGCCTCGTC  
.....  
4151 ACAAGCCCGT CAGGGCGCGT CAGCGGTGT TGGCGGGTGT CGGGGCTGGC  
TGTTCCGGCA GTCCCGCGCA GTCGCCACA ACCGCCACA GCGCCGACCG  
.....

ApaLI  
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4201 TTAACATGCG GGCATCAGAG CAGATTGTAC TGAGAGTGCA CCATATCGAC  
AATTGATACG CCGTAGTCTC GTCTAACATG ACTCTACGT GGTATAGCTG  
.....  
4251 GCTCTCCCTT ATGCGACTCC TGCATTAGGA AGCAGCCAG TAGTAGGTTG  
CGAGAGGGAA TACGCTGAGG ACGTAATCCT TCGTCGGGTC ATCATCCAAC  
.....  
4301 AGGCCGTTGA GCACCGCCGC CGCAAGGAAT GGTGCATGCA AGGAGATGGC  
TCCGGCAACT CGTGGCGGCG GGTTCCTTA CCACGTACGT TCCTCTACCG  
.....  
4351 GCCCAACAGT CCCCCGGCCA CCGGGCCTGC CACCATACCC ACGCCGAAAC  
CGGTTGTCA GGGGCGCGT GCGCCGACG GTGGTATGGG TGCGGCTTTG  
.....  
4401 AAGCACTAAT AGGAATTGAT TTGATGGTA TAAACGAAA CAAAAAAG  
TTCGTGATTA TCCTTAATA AACCTACCAT ATTGCCTTT GTTTTTTTC  
.....

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FIG. 8. (CONTINUED)

4451 AGCTGGTACT ACTTCTTTA AATTATTTT ATTATTGAT TTTATTTAAT  
TCGACCATGA TGAAGAAAT TTTAATAAAA TAATAAACTA AAATAAATTA  
.....

4501 AGTATATATT ATATTTTGAA CGTAGATTAT TTTGTTGAAA GTTGCTGTAG  
TCATATATAA TATAAACTT GCATCTAATA AAACAACCTT CAACGACATC  
.....

4551 TGCCATTGAT TCGTAACACT AATTCTGTAT TAGTCATTCC TCTTGTTTGA  
ACGTAACATA AGCATTGTGA TTAAGACATA ATCAGTAAGG AGAACAACT  
.....

4601 TAGTATCCAA AAAACGGCT ATTTTTTTC AATCTTATT CCTGCATATT  
ATCATAGGTT TTTTGCCGA TAAAAAACG TTAGAATAAA GGACGTATAA  
.....

4651 ATACAGATAA CATAATGAAA GAAAAATCT TTTTTTTGT TCTTCAATGA  
TATGTCTATT GTATTACTTT CTTTTTGA AAAAAACA AGAAGTTACT  
.....

4701 TGATTTCAAC CATTCTTTA AACATTGATC AATCCTGAG CAACAACCC  
ACTAAAGTTG GTAAGAAAT TTGTAAC TAGTAAAGCTC GTTGTGGGG  
.....

4751 ATACACACTG GTTATATAC CGCCCTTTT ACAGTTGAAG AAAGAAATAG  
TATGTGTGAC CAAATATATG GCGGGGAAAA TGTCAACTTC TTTCTTTATC  
.....

4801 AAATAGAAAT AGCAACAAA AGATATGACA GTCAACACTA AGACCTATAG  
TTTATCTTTA TCGTTTGTG TCTATACTGT CAGTTGTGAT TCTGGATATC  
.....

4851 TGAGAGAGCA GAAACTCATG CCTCACCAGT AGCACAGCGA TTATTCGAT  
ACTCTCTCGT CTTTGAGTAC GGAGTGGTCA TCGTGTGCT AATAAAGCTA  
.....

4901 TAATGGAAC GAAGAAAACC AATTATGTG CATCAATTGA CGTTGATACC  
ATTACCTTGA CTTCTTTTG TAAATACAC GTAGTTAACT GCAACTATGG  
.....

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4951 ACTAAGGAGT TCCTCGAGT AATTGATAA TTAGGTCCTT ATGTATGCTT  
TGATTCCTCA AGGAGCTCA TAACTATTT AATCCAGGAA TACATACGAA  
.....

5001 AATCAAGACT CATATTGATA TAATCAATGA TTTTCCTAT GAATCCACTA  
TTAGTTCTGA GTATACTAT ATTAGTTACT AAAAAGGATA CTTAGGTGAT  
.....

5051 TGAACCAATT ATTAGAATT TCACGTAAAC ATCAATTTAT GATTTTGA  
AACTTGGTAA TAATCTGAA ATGCAATTG TAGTTAAATA CTAATAACTT  
.....

5101 GATAGAAAAT TTGCTGATAT TGGTAATACC GTAAAGAAAC AATATATTGG  
CTATCTTTA AACGACTATA ACCATTATGG CATTCTTTG TTATATAACC  
.....

5151 TGGAGTTTAT AAAATTAGTA GTTGGGCAGA TATTACCAAT GCTCATGGTG  
ACCTCAAATA TTTAATCAT CAACCGTCT ATAATGGTTA CGAGTACCAC  
.....

5201 TCACTGGGAA TGGAGTGGT AAGGATTAA AACAGGGAGC TAAAGAAACC  
AGTGACCTT ACCTACCAA CTCCTAATT TTGTCCTCG ATTTCTTTGG  
.....

5251 ACCACCAACC AAGAGCCAAG AAGGTTATTG ATGTTAGCTG AATTATCATC  
TGGTGGTTGG TTCTCGGTTT TCCCAATAAC TACAATCGAC TTAATAGTAG  
.....

5301 AGTGGGATCA TTAGCATATG TGAATATTC TCAAAAACT GTTGAAATTG  
TCACCCTAGT AATCGTATAC CTCTATAAG AGTTTTTGA CAACTTAAAC  
.....

5351 CTAATCCGA TAAGGAATT TTTATTGGAT TTATTGCCA ACGTGATATG  
GATTAGGCT ATTCCTTAA CATAACCTA AATAACGGGT TGCATATAC  
.....

FIG. 8. (CONTINUED) 25/63

5401 GGTGGCCAAG AAGAAGGATT TGATTGGCTT ATTATGACAC CTGGAGTTGG  
CCACCGGTTT TTCTTCCTAA ACTAACCGAA TAATACTGTG GACCTCAACC  
.....  
5451 ATTAGATGAT AAAGGTGATG GATTAGGACA ACAATATAGA ACTGTTGATG  
TAATCTACTA TTTCCACTAC CTAATCCTGT TGTATATCT TGACAACTAC  
.....  
5501 AAGTTGTTAG CACTGGAACAT GATATTATCA TTGTTGGTAG AGGATTGTTT  
TTCAACAATC GTGACCTTGA CTATAATAGT AACAACCATC TCCTAACAAA  
.....  
5551 GGTAAAGGAA GAGATCCAGA TATTGAAGGT AAAAGGTATA GAAATGCTGG  
CCATTTCCTT CTCTAGGTCT ATAACCTCCA TTTTCCATAT CTTTACGACC  
.....  
5601 TTGGAATGCT TATTTGAAAA AGACTGGCCA ATTATAAATG TGAAGGGGGA  
AACCTTACGA ATAACTTTT TCTGACCGGT TAATATTAC ACTTCCCTCT  
.....  
5651 GATTTTCACT TTATTAGATT TGTATATATG TAGAATAAAT AAATAAATAA  
CTAAAAGTGA AATAATCTAA ACATATATAC ATCTTATTTA TTEATTATT  
.....  
5701 GTTAAATAAA TAATTAAATA AGGGTGGTAA TTATTACTAT TTACAATCAA  
CAATTTATTT ATTAATTTAT TCCACCATT AATAATGATA AATGTTAGTT  
.....  
5751 AGGTGGTCCT TCTAGCTGTA ATCCGGGCG AGCAACGGAA CATTCATCAG  
TCCACCAGGA AGATCGACAT TAGGCCCGTC GCGTTGCCCT GTAAGTAGTC  
.....  
5801 TGTAATAAATG GAATCAATAA AGCCCTGGCG TCATGAGCCC GAAGTGGCGA  
ACATTTTAC CTTAGTTATT TCGGGACCGG AGTACTCGGG CTCACCGCT  
.....  
5851 GCCCGATCTT CCCCATCGGT GATGTGGCG ATATAGGCGC CAGCAACCGC  
CGGGCTAGAA GGGGTAGCCA CTACAGCCGC TATATCCGC GTGCTTGGCG  
.....  
5901 ACCTGTGGCG CCGCAGCGCG CAGGGTCAGC CTGAATACGC GTTTAATGAC  
TGGACACCGC GGCGTCGCG GTCCTAGTC GACTTATGCG CAAATTACTG  
.....  
5951 CAGCACAGTC GTGATGGCAA GGTGAGAATA GCCCAAGTC GCGAGGGGC  
GTCGTGTCAG CACTACCGTT CCAGTCTTAT CCGGTTTACG CCGCTCCCCG  
.....  
6001 CTGTACAGTG AGGGAAGATC TGATATTGAC GAAGAGGAAC CAATGTAACG  
GACATGTCAC TCCCTTCTAG ACTATAACTG CTTCTCCTTG GTTACATTGC  
.....  
6051 TTACACTGAA GAAACACAC AATAAACGGG AAGAAACGGT GTAAAGTGT  
AATGTGACTT CTTTGTGTG TTATTGCCC TTCTTTGCCA CATTTCACA  
.....  
6101 GAAAATAATT TTTGAATATC ATTCCCTTG GTTTAATTCC AAACGAAACG  
CTTTATTAA AACTTATAG TAAAGGGAAC CAAATTAAGG TTTGCTTTC  
.....

EcoRI

6151 TGTTTTTTTT AGAGAATGGG AATTCCTATT GGATGTCTAG ATTGTTTGT  
ACAAAAAAA TCTCTTACCC TTAAGAATAA CCTACAGATC TAACAAACAA  
.....

ApaLI

6201 TACTCCAGAC TGTGCACAAA AACGTTTGA TGGATGATCA GAAGATATTT  
ATGAGGTCTG ACACGTGTTT TGGCAACCT ACCTACTAGT CTTCTATAAA  
.....  
6251 TTAGGCTTAG CTCTAAATAT AAGAAATGAT GCTTGAAAAA CCAGACAGAA  
AATCCGAATC GAGATTTATA TCTTTACTA CGAATTTTT GGTCTGTCTT  
.....  
6301 ATTGAGTTTC AAAAATTGGT AATGTGAGGT ATTAGTCAAC TAACCAATA  
TAACTCAAAG TTTTAACCA TTACACTCCA TAATCAGTT ATTGTTTAT  
.....

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## FIG. 8. (CONTINUED)

6351 ACAATGC AAA CCGGTTGATA CATTTCATTT TGAAAATAAT GAAACTGGAA  
TGTTACGTTT GGCCAAC TAT GTAAAGTAAA ACTTTTATTA CTTTGACCTT

6401 TTGGATGACC AGCACACAAA CACATAAAGT AATTATGGGA ATTAGAAGCG  
AACCTACTGG TCGTGTGTTT GTGTATTTCA TTAATACCCT TAATCTTCGC

6451 AACATAGAGG AGTACTTGGC CACGAACAGA ATACAAGTGG GAACACTATT  
TTGTATCTCC TCATGAACCG GTGCTTGTCT TATGTTTACC CTGTGATAA

6501 TTCTCCATTG TTTAGTTCT GTTTTTTGT CAGCCTAGTT TTGTGCTATG  
AAGAGGTAAC AAAATCAAGA CAAAAAACA GTCGGATCAA AACACGATAC

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6551 TGTAAAAAAT ATTGCCAAGA AAAAAGCTT GTTTTGTGGC CAGTGTCCGA  
ACATTTTTTA TAACGGTTCT TTTTTCGAA CAAAACACCG GTCACAGGCT

6601 AAAAAATTTT GGGGAATCTT CGGATTAAAT TATGTTTTCA  
TTTTTTAAAA CCCCTTAGAA GCCTAATTAA ATACAAAAGT

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FIG. 9.

ATGTATGTTTATAAGAGAGATGGCCGTAAAGAGCCAGTACGTTTCGACAAAAT  
CACTGCCAGAGTTCAAAGATTATGTTA  
CGGTTTGAATCCAAACCACGTTGAACCAGTTGCTATTACCCAAAAAGTTATATC  
AGGTGTTTACCAGGGGGTACTACTA  
TTGAGTTGGACAACTTGGCTGCAGAAATTGCTGCTACAATGACAACAATTCAC  
CCAGATTACGCTGTCTTAGCCGCTAGA  
ATTGCCGTATCAAATTTACATAAGCAAACCACCAAACAGTATTCCAAAGTGTC  
TAAGGATTTATATGAATACATTAATCC  
TAAGACTGGGTACACTCTCCTATGATTTCCAAGGAAACCTACGACATCATTAT  
GGAACACGAAGATGAATTAACCTCAG  
CCATTGTTTACGACAGAGATTTAACTACAATTATTTTGGGTCAAGACTTTGG  
AAAGATCATATTTGTTACGTATCAAC  
GGTAAGGTTGCTGAAAGACCACAACATTTGATCATGAGGGTTGCTGTCCGGTAT  
TCACGGTAATGATATACCAAGGGTCAT  
TGAAACCTATAACTTGATGTCTCAAAGATTCTTCACCCATGGTTCTCCTTGTTTA  
TTTAACGCTGGTACACCAAGACCAC  
AAATGTCCTCATGTTTCTTGCTTGCTATGAAGGATGATTCTATTGAAGGTATTT  
ACGACACTTTGAAATCGTGTGCTTTG  
ATCTCAAAAAGTGCTGGAGGAATCGGTTTACACATCCACAACATTCGTTCTACC  
GGTGCTTACATTGCTGGTACCAATGG  
TACTTCTAATGGTATTATTCCAATGGTAAGAGTATTCAATAAACTGCACGTTA  
TGTCGACCAAGGTGGTAACAAGAGAC  
CTGGTGCCTTTGCCTTGACTTAGAACCATGGCACAGTGACATTTTTGATTICA  
TTGATATTAGAAAGAATCACGGTAAA  
GAAGAAATCAGAGCCAGAGATTTGTTCCCAGCTTTGTGGATTCCAGATTTGTTT  
ATGAAAAGAGTTGAACAAAATGGTGA  
CTGGACTTTATTCTCACCAAATGAGGCCCCAGGCTTGGCTGATGTTTATGGTGA  
CGAATTCGAAGAATTATACACCAAAT  
ACGAAAAAGAAAACCGTGGTAGACAGACCATCAAAGCTCAAAAATTGTGGTA  
TGCTATTTTGGGAGCCCAAACCTGAAACA  
GGTACCCCATTTATGTTATATAAAGATTCATGTAACAACAAATCCAACCAAAA  
GAACTTGGGTATTATCAAATCTTCAA  
CTTGTTGTGAAATTGTTGAATATTCTGCTCCAGATGAAGTTGCTGTTTGTA  
CTTGGCTTCCATTGCCTTGCCATCAT  
TTGTTGAAAATGATGAAAAAGTACTTGGTACAACTTTGACAAATTACATCAG  
GTCATAAGGTTGTACCCGTAACCTTG  
AACAGAGTTATTGACCGTAACCATTACCCAGTCCCAGAAGCTGAAAGATCAAA  
CATGAGACACAGACCAATTGCTTTGGG  
TGTTCAAGGTTTGGCTGATGCCTTTATGGAATTGAGATTACCATTTGACTCTCA  
AGAAGCTAGAGAATTGAACATTCAAA

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## FIG. 9. (CONTINUED)

TTTTTGAGACTATCTACCATGCTGCTGTTGAAGCTTCAATTGAATTGGCTAAAG  
AAGAAGGTGCCTACGAAACCTATCCA  
GGTTCTCCAGCCTCTCAAGGTTTATTACAATTTGATTTGTGGAACAGAAAACCA  
ACTGAATTATGGGATTGGGATACATT  
AAAACAAGATTTGGCCAAACATGGTATGAGAACTCCTTGTTGGTTGCACCAA  
TGCCTACTGCTTCCACATCACAATTT  
TGGGTAACAATGAATGTTTTGAACCATACACTTCTAACATTTACTCTAGAAGAG  
TATTAGCTGGAGAATTCCAAATTGTC  
AATCCATATTTATTGAAGGACTTGGTTGATTTGGGTGTCTGGAACGACGCTATG  
AAAAGTAGTATTATTGCTAACAATGG  
TTCTATCCAAGCCTTACCAAACATCCCTGATGAAATCAAGGCATTGTACAAAA  
CTGTCTGGGAAATCTCACAAAAACATA  
TTATCGACATGGCTGCTGATAGAGCAGCATTTATTGATCAATCTCAATCATTAA  
ACATTCACATCAAAGATCCAACAATG  
GGTAAATTAACCAGTATGCACTTCTACGGTTGGAAGAAAGGTTTAAAGACTGG  
TATGTACTACTTAAGAACACAAGCTGC  
CAGTGCTGCTATTCAATTTACCATTGATCAAAAGATTGCTGAGACTGCCGGTCA  
TACGGTTGCCAACTTGGACAAATTAA  
ACATTAAGAAATATGTTAACAAAGGAAGAGTTGAGAGTGAGAATACCAGTGAT  
GCTCCATACAAGTCACCATCAACCGAA  
CCAACCTCATTAGAAAGTTCAGTTGCTGATTTGAAAATAAAAGATGAAGGTGA  
AAAGCCAGCTGAAGACAAAACCATTGA  
AGAAGTCGAAAATGACATTTATAGTGCCAAAGTTATCGCATGTGCTATTGATA  
ATCCAGAATCTTGTACAATGTGTTCTG  
GT

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FIG. 10.

ATAGAAGCTGTTTGATATACAACTATCTCACTCCCAATTGTGACTTGAAATAATAATAATACCTATCACCTAGTAATCTTT  
ATCTTAACGTAACTCTGCAAGCACAATCAATGTATAAAGCATAAAGATAAATCTTGGTGAGGTTTAAATTCAATAAT  
TATAATGAACACAAATTACTAAAGGCAATGGTATCAACAAATTTATAGGCTAGGTAGAACCATAGTGCTGTTCGGGAGTT  
CGGTAGTTTGGGAAGTTGGGAAGTTGGATAGTTTGAGAAAGTTCCGTGCTGATCTAAATTAACAGAGAACGATAT  
AATGTACAAATAACATTCAGAAATTTAAACAACCTTTATATATATATAATAATGCTCTTGTCATCAACTTGCCATTGC  
TGTGATGATGCTTTCCTGTTAAATATACCTTTAAGAACCAGATTCACATCTCAACTAATAATTAACCTTATACCTTTT  
GTTTGACATTCCTAATGACACAAAGAATGTGAAATAATTTAGCCTCAAGGGATCTACTCATTCCTCTCAAAACA  
CACATTCCTTTGTATCACCAATACCTTTTGTAAACAGAGGAACAAATAATGACACGGCATGTCAATTAACCTATAGGACTA  
TCACTACAAATCAAGGATTTACAAATAGTGGCAATGTCAAAATCATGTATATTTAAACACATTAACACATATTTATTTCA  
GGTACATAATACTCAATATCTAAATTTCAAAATGGTACTGTACCTTAACTTCTCCTTCATGTCTAGTTGATATATTAT  
ACTTGCTAAATGTCAAAATAATCATGTCTTCACACATTCAGGTTGT

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FIG. 11.

SCAAGATCTAACTCCAGTTTTTTGGTGTATGTTACACAGCAACAAATATAATCGAAAGAGCCCAATATTCT  
CTTCTACAAATTACGAAATATGTTTCACA:GTATGAAGAGCTTTATCTATACTATTTCTCCTCCAACTCTAGCAGTGAG  
AATGATACCTGATATCTCCTAT:AGGATACAGTTATCTATTATAGTATATAATATCATGGAGATAATATATTAAA  
TCGATGGAGTTAAGGAGAAACAAATACACCCCAATTTGCGAGCAAAATGAGACATTTTCACAGAAAGAAACCAAGAAAG  
ACAATTACTCCATTCAATAATTCACAA:AAAAAATAACAAGAACAAAGTACTAACAAACATCAGTAATTTCA  
CTTTGAAATCTTTACATAGTCAAGTTCTAAAGATTAAATATAGCGATGCAATTTTCATCAGAAATTTAGTGTATACAATA  
TGCAGGTGATTATGAGCCAGGTGAACAA:TCCTTACTAAAAATCTAGGAGTTGTTTATATACAGTATTTTGTCTAAC  
GTGTCTCTAACGTATACAGATAGATTGTAATCGGTTAGAAATACAGAAAGGTTGTTGTGGACCTTGGTGGTGG  
GAAATTTGAATGATATAATTGTTATCTCAAGTATAGCAAAATACAGGCAAGGTTGCAACAAACCAAGAACTTGGATT  
GTCCGAATTTCTCTTCACCCCTT:CAGAAATG:CCTCGTGTATGTGATCAAT



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FIG. 12.

CCCCGTTAACCACTTCTAGGGTATACCATTTTCATCTGACTGAATAACTGGTTAG  
TCGATTTGTTGTTGAAGAAAAGTGAC  
CACCTAGTTTTTTCTGCCAACATTTTTTGCGATGAGCCGTCGACGCGTTGTCTTT  
TTCTACCCACGTTTAACAATCTTG  
CCAGTCAATTCCTAGCCAAATAAACTTTAGACTCACAACCTCTAACACTGACTC  
GTGCCCCCCTGTTTAAACTCTAAATT  
ACTTCACAGAGCCTTTACTACCTTAAATTTARGRTTWTSKAKKGTTTCTGTTTTT  
TTGCAAATCACCTGACTYGTTTTT  
TTTTCAGCCAGGTTTTTCGTTAAAATCTGACCAAAAAATTTACRACTCCTATWT  
TTAAAACCTCYAAAWWACAATTAAAC  
TCAATTCAGACAAGTCCTTCTGCTCATTCTGAGTCTTCTCTATTGTCTTTTGACT  
TTTTGTGTGTGACTATTTTCATGAT  
CACCCCGTTTCTTGCATTTTTTTCAGTCAACTTTTTCTCAAATCAAGCCAAAAA  
AACACACCTTTAACTACCTATACAA  
CGCAAACCTATTCAAAACA

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FIG. 13.

ATGACTACTTCCAAGGAACTTTCCTTTTCACTTCAGAATCCGTTGGTGAAGGT  
CACCCAGATAAGATTGTGACCAAGT  
CTCCGATGCCATTTTAGATGCTTGTTTAGCTGTTGATCCATTGTCAAAAGTTGCT  
TGTGAAACTGCTGCCAAAACCGTA  
TGATTATGGTTTTTGGTGAAATTACCACTAAAGCTCAATTGGATTATCAAAAAA  
TCATTAGAGACACCATTAAACACATT  
GGTTACGACGATTCTGAAAAAGGTTTIGATTACAAGACTTGTAACGTCTTGGTT  
GCAATTGAACAACAATCTCCAGATAT  
TGCTCAAGGTTTACATTACGAAAAAGCTTTGGAAGAGTTGGGTGCTGGTGATC  
AAGGTATTATGTTTGGTTATGCCACCG  
ATGAAACCGATGAAAAATTGCCATTGACCATTTTATTGGCCACAAATTGAAT  
GCTGCCTTGGCTTCTGCCAGAAGATCA  
GGTTCCTTGCCATGGTTGAGACCAGATACCAAAACCCAAGTCACCATCGAGTA  
TGAAAAAGATGGTGGTGCAGTTATCCC  
AAAAAGAGTCGACACAATTGTTATTTCCACTCAACATGCCGAAGAAATCACCA  
CCGAAAATTTGAGAAAAGAAATTATTG  
AACATATCATCAAGCAAGTCATCCCAGAACATTTATTAGACGACAAAACCTATC  
TACCACATTAGCCATCAGGCAGATTC  
GTCATTGGTGGTCCCCAAGGTGATGCTGGTTTGACTGGTAGAAAGATCATTGTT  
GACACCTATGGTGGTTGGGGTGACA  
TGGTGGTGGTGCCTTCTCAGGCAAGGATTTCTCCAAAGTTGATAGGTCTGCTGC  
TTATGCCGCTCGGTGGGTGCTAAGT  
CGTTGGTGACCGCCGATTGGCCAAAAGGGCCTTGGTGCAGTTCTCCTATGCTA  
TTGGGGTTGCTGAACCCACCAGCATT  
TATATAGACACCTATGGGACATCTAAATTGAGCACCGAAGCCCTTGTAGAAAT  
TATCAAGAATAATTTTGA CT TACGCCC  
TGGCGTAATTGTAAAAGAATTAGATTTGGCTCGTCCTATTTATTTTAAAACCGC  
TTCTTACGGACATTTTACTAACCAAG  
AAAATTCTTGGGAACAACCAAAAAAATTAAAATTT

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FIG. 14.

1 MYVYKEDGRX EFVRFCKITA KVGRLCYGLN P:HVPEVAIT QKVISGVYQG  
 31 VTTIELDNLA AELAAITMTTI HPOZAVLAAR IAVENLHKQT TKQYSKVSKE  
 101 LYEYINPKTG LHSFMISKET YDILMEHZEDE LNSAIVYDRD FNYNYFGFKT  
 151 LERSYLLRIN GFWAERPQHL IMPVAVGZHG NDIFRVIETV NLMSQRFTTH  
 201 GSPCLFNAOT FRPQMSSCTL LAMKDDSTEG IYDTLKSCAL ISKSAGGIOL  
 251 HINNIRSTGA YIASTINGTSH GIIPMVVVFVN NTARYVDJGG NKZPGAFALY  
 301 LEFWHSDIFD FIDIRKWHGX BEIRARDLFP ALWIPDLFMK RVEQNGEWTL  
 351 FSPNEADOLA EYVGCEFEEL YTKYEKENRG RQTIKAQKLW YAILGAYTET  
 401 GTFFMLYADS CEXSNQKNL GIIKSSNLCC EIVEYSAPDE VAVCNLASIA  
 451 LPSFVENDKX STWTFEKLH QVTKVVTREL NRVIDRNHYF VPEAERSNMR  
 501 HRPIALGVQG LACAFMEIRL PFDSQEAREL NIQCFETIYH AA/VEASIELA  
 551 KEEGAYETYP GSPASQCLLQ FDLNWKKFTS LWDWDTLXQD LAXHGNRNSL  
 601 LVAPMPTAST SIZLGNIECF EPYTSNIYSE RVLAGEFGIV NPYLZDLVD  
 651 LGVANDAKES SIINNGSIQ ALPNIPDEIK ALYKTVWEIS QKHTIDMAAD  
 701 RAAFIDQSQS LNNEXDPTX GKLTSMHFTG WKXGLKTGMY YLRTQAASAA  
 751 IQPTIDQKIA ETASHIVANL DELNIXKYVN KGRVESENTS DAPYKSTSTE  
 801 PTSLESSVAC LXXDEGEKF AEDKTIEZLE NDIYSAXVIA CAIENPESCT  
 851 KCSG

*34/63**FIG. 15.*

1 MITSKZTFLE TSESVEZCHF DKICDQVSDA ILDACLAVER LSKVACETAA  
51 KTGXIN/EGE ITTKAQLD/Q KZIFDTIKH GYDSEKGFY YATCNVLVAI  
101 EQOSPDIAG LHYKALBBL GAGDQGINFG YATDETDEKL PETILLAKKL  
151 NAALASARNS GELFWLRDPT KTQUTIEYK DGGAVIPERV DTIVISTQHA  
201 EEITTENLRY ETEHIIKQV IPEHLLDOKT IYHIQPSGRF VIGGFQGEAG  
251 LTGRKIIVET YGGMJAHCCG AFSCNDFSKV DRSAAYAARN VAKSLUTAGL  
301 AKKALVQFSY AGVAREPTSE YTDYGTSL STEALVETIK MTFDLRPGVI  
351 VZELDLARPE YTKASVGHF TNQENSWECP KXKLF

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FIG. 16.

RH170498 AF101-AF150 (16 hours  
glucose/maltose vs galactose/maltose  
AF110

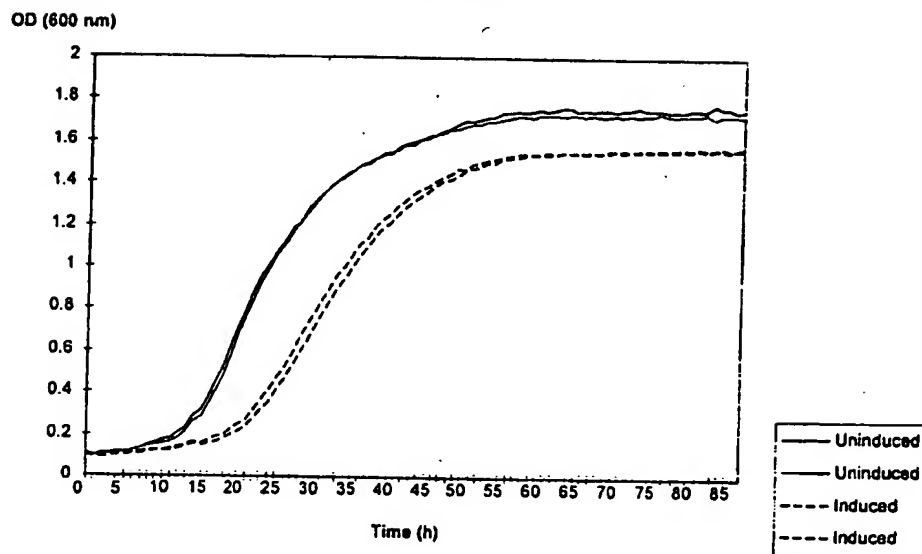
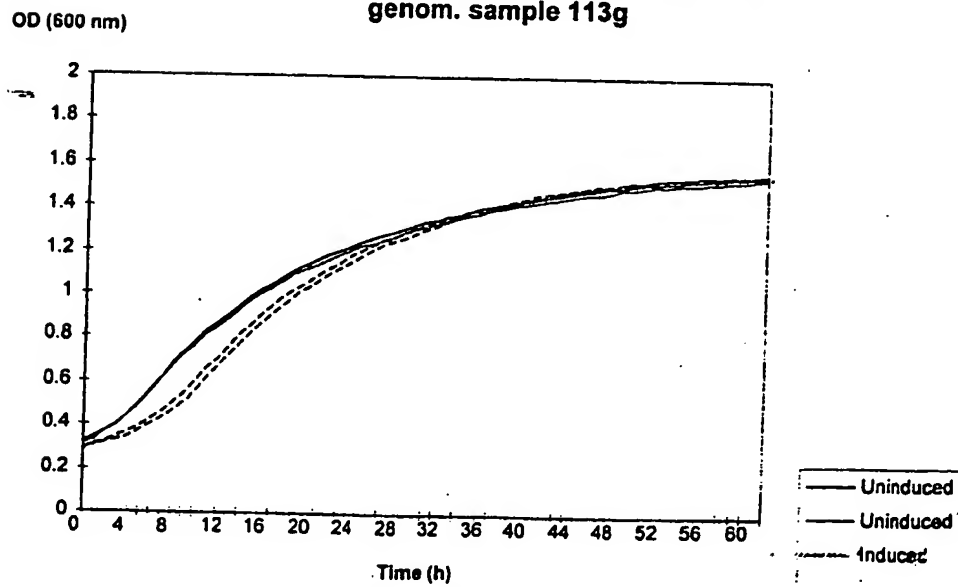


FIG. 17.

C. albicans library screening experiment 28/11/97  
glucose/maltose vs galactose/maltose  
genom. sample 113g



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FIG. 18.

RH170498 AF101-AF150 (16 hours induction).  
glucose/maltose vs galactose/maltose  
AF117

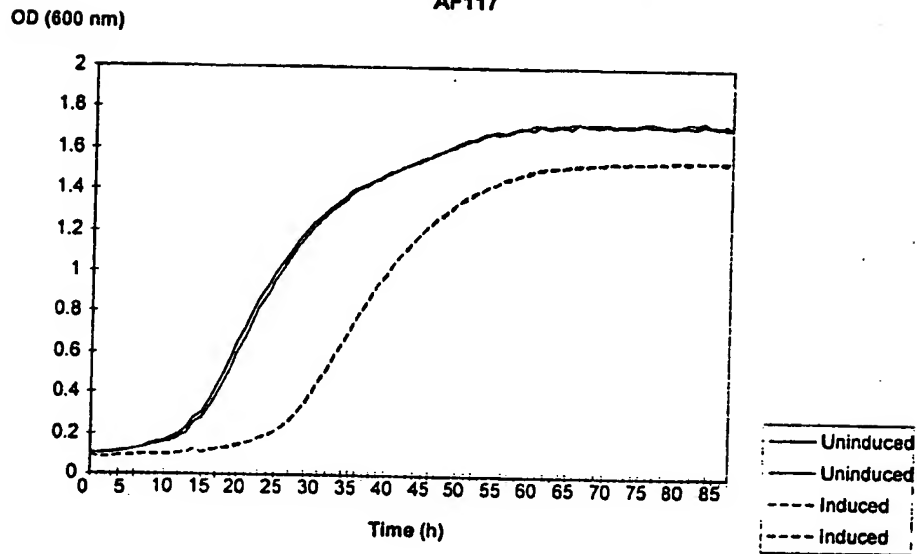
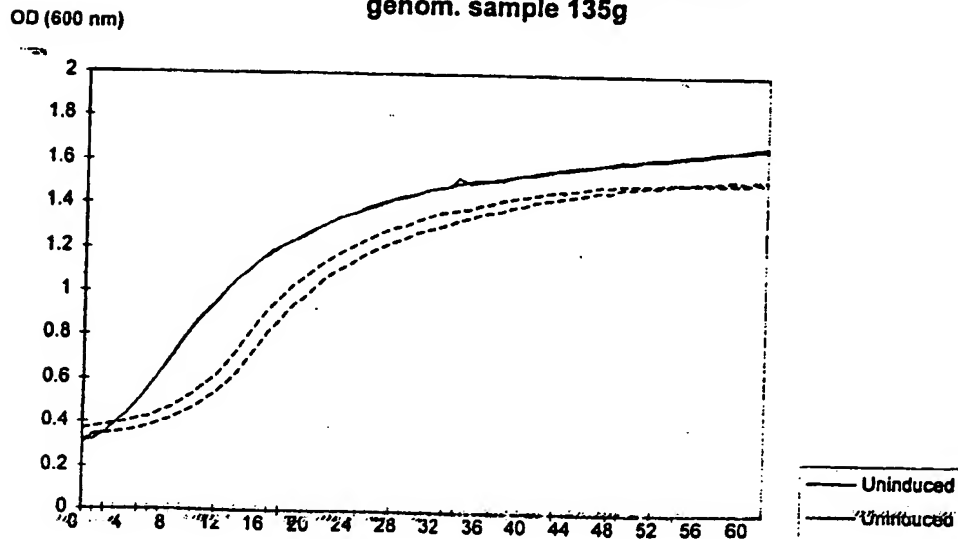


FIG. 19.

C. albicans library screening experiment 28/11/97  
glucose/maltose vs galactose/maltose  
genom. sample 135g



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FIG. 20.

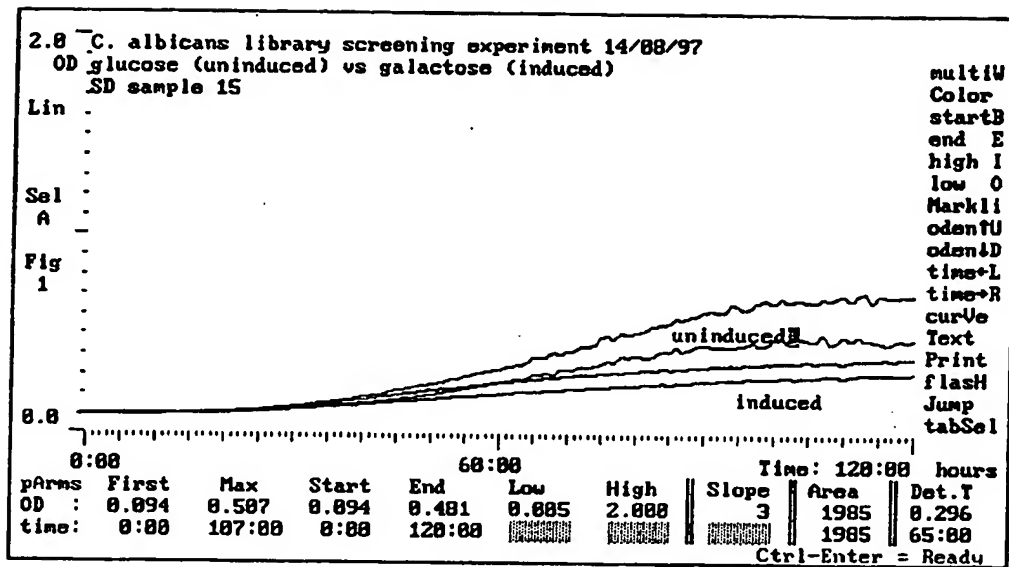
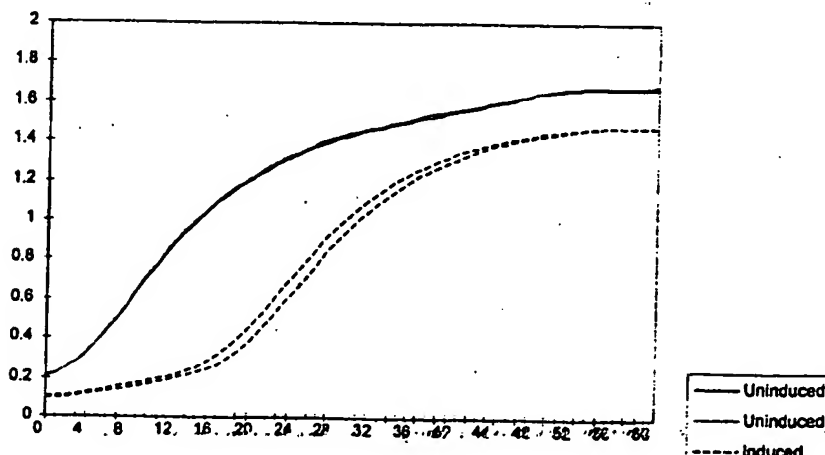


FIG. 21.

C. albicans library screening experiment 31/03/98  
glucose/maltose vs galactose/maltose  
sample 17CP

OD (600 nm)



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FIG. 22.

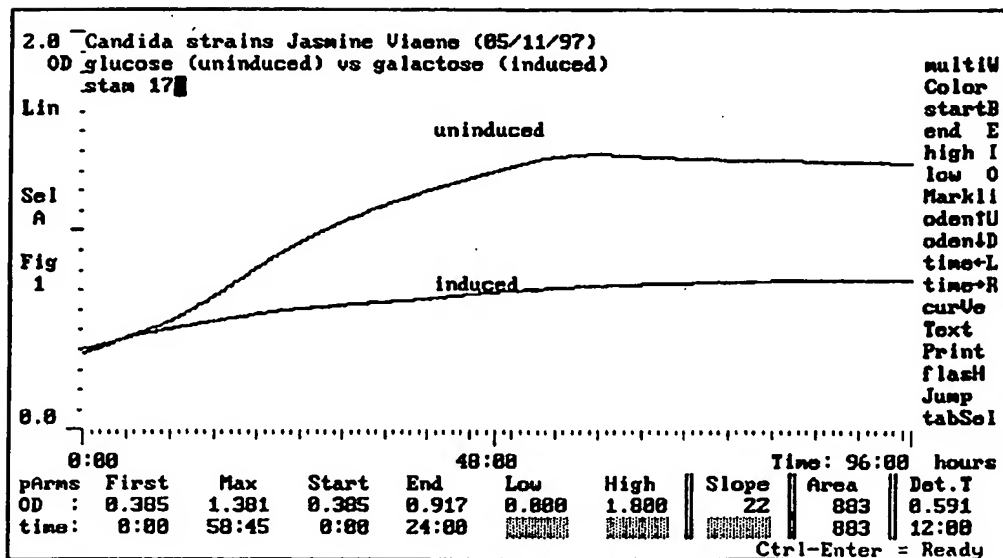
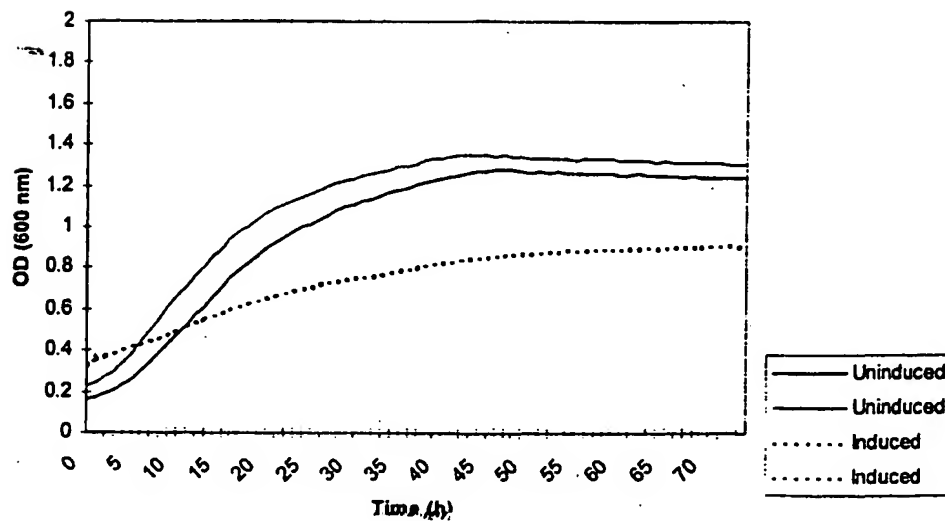


FIG. 23.

C. albicans library screening experiment 15/12/97  
 glucose vs galactose  
 genom. sample 190g





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FIG. 24.

C. albicans library screening experiment 15/12/97  
glucose vs galactose  
genom. sample 207g

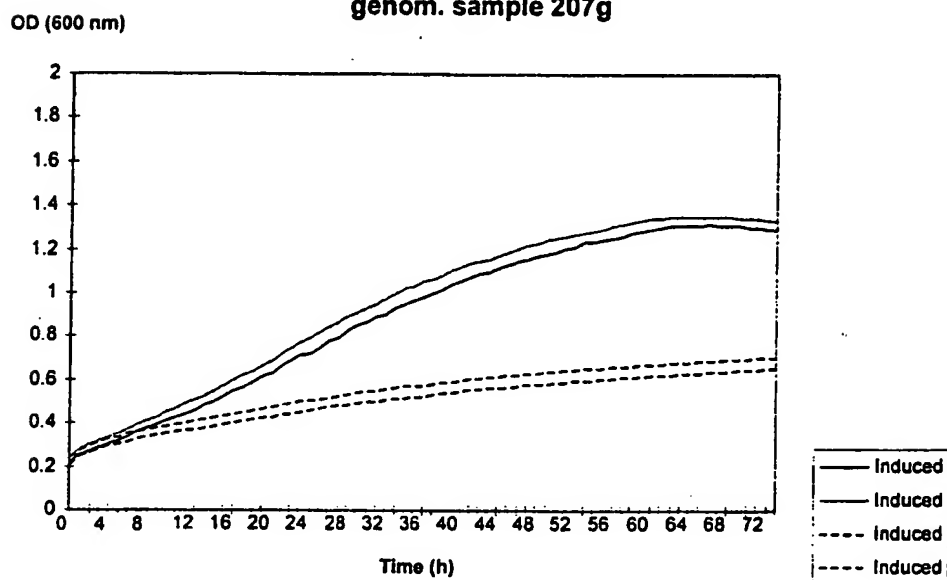
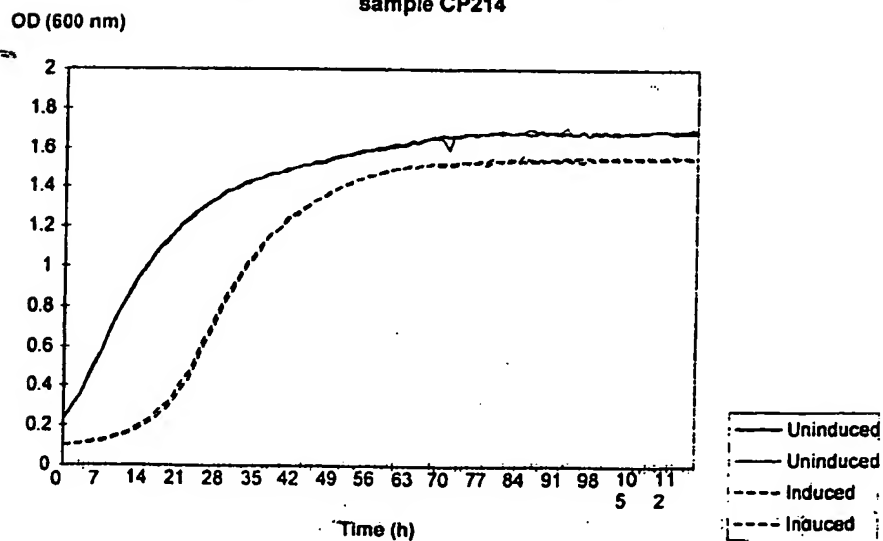


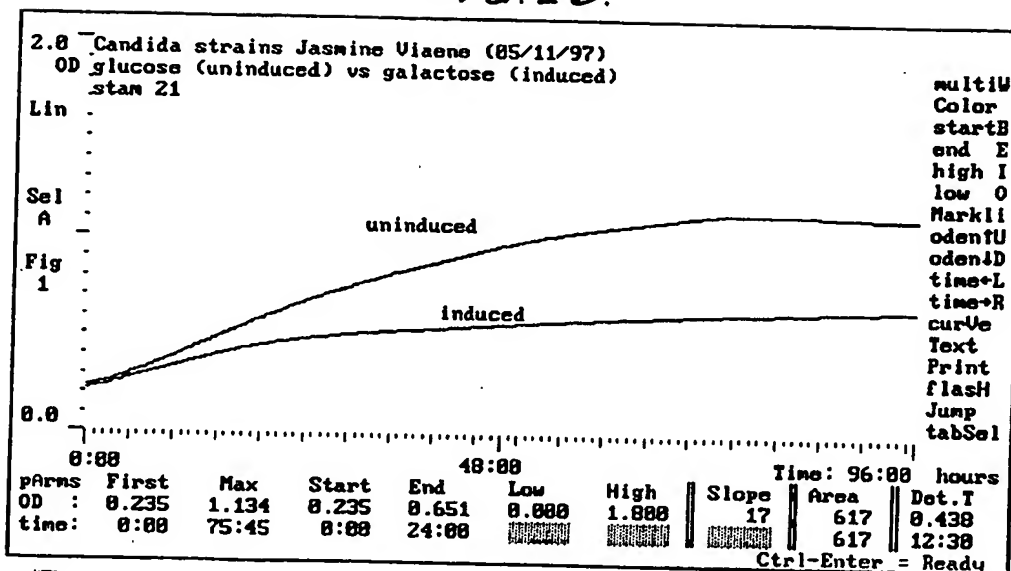
FIG. 25.

CP211-234+AF231-254 28/04/98 IVR  
glucose/maltose vs galactose/maltose  
sample CP214



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FIG. 26.



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FIG. 27.

C. albicans library screening experiment 15/12/97  
glucose vs galactose  
genom. sample 222g

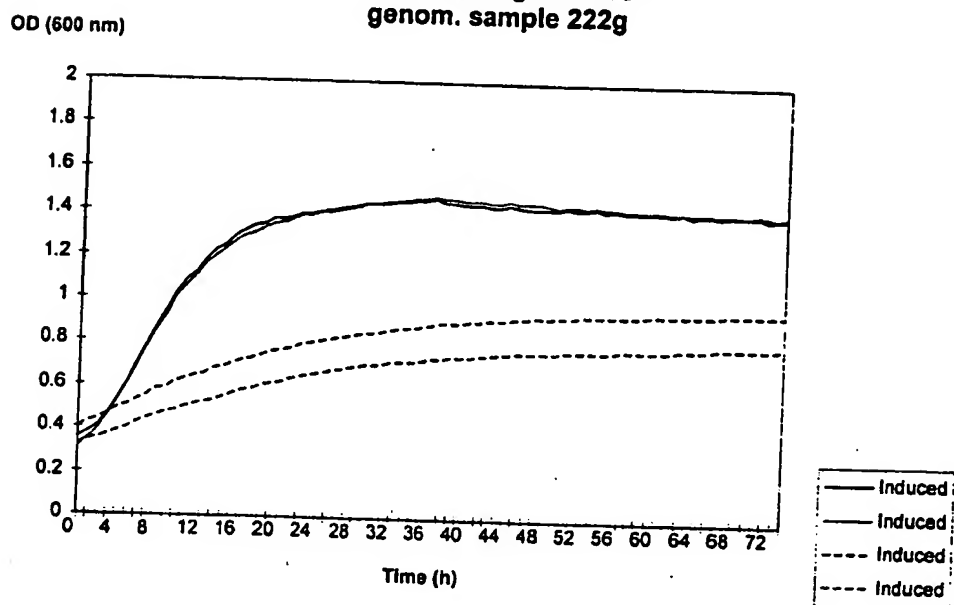
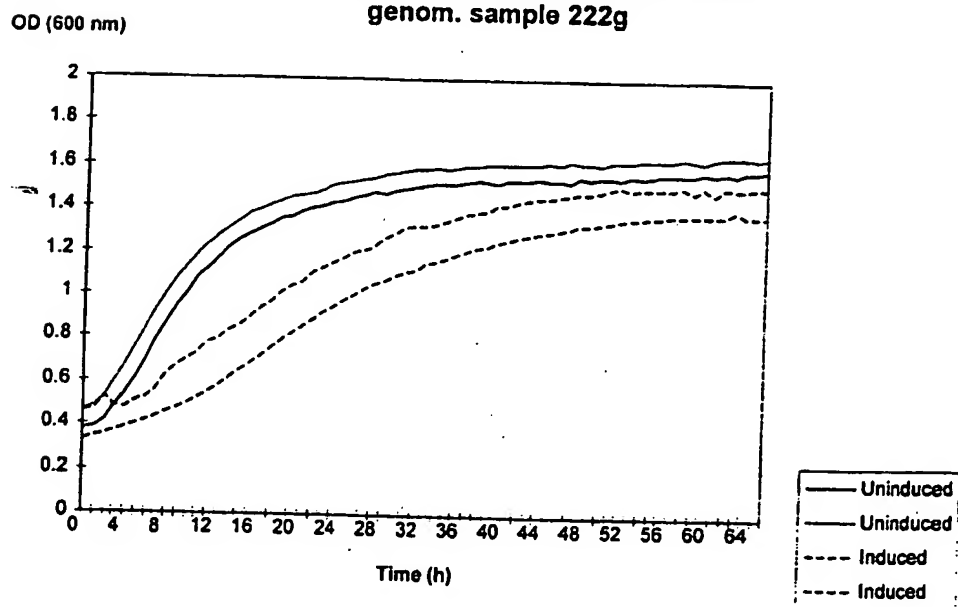


FIG. 28.

C. albicans library screening experiment 19/12/97  
glucose/maltose vs galactose/maltose  
genom. sample 222g



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FIG. 29.

CP211-234+AF231-254 28/04/98  
glucose/maltose vs galactose/maltose  
sample CP223

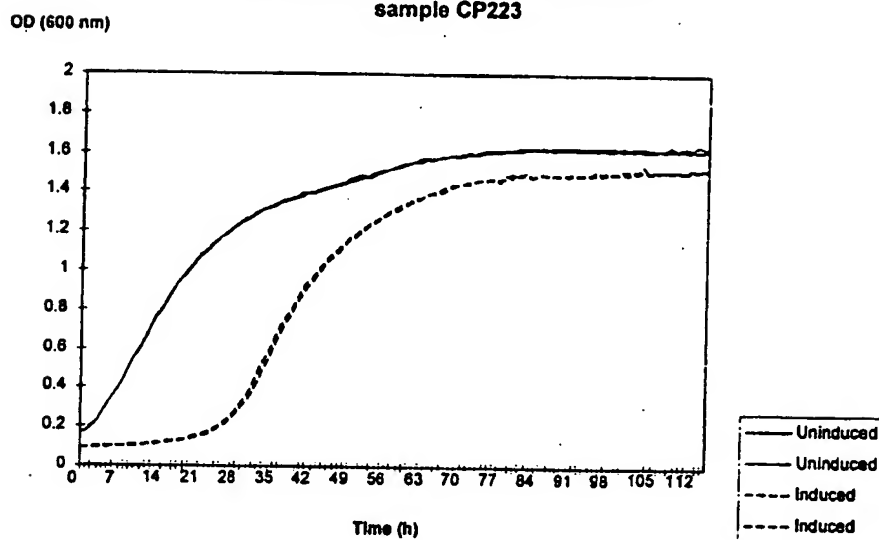
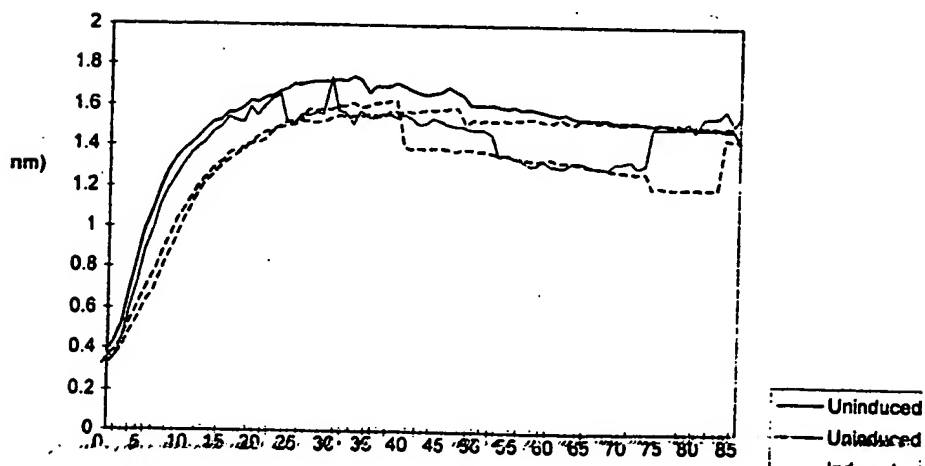


FIG. 30.

C. albicans library screening experiment 24/04/98  
glucose/maltose vs galactose/maltose  
sample 226af



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FIG. 31.

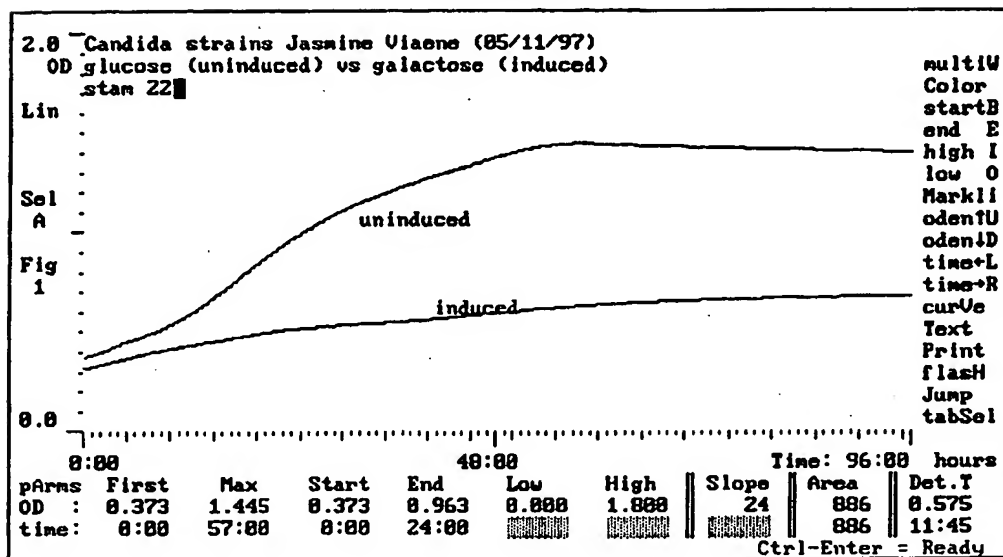
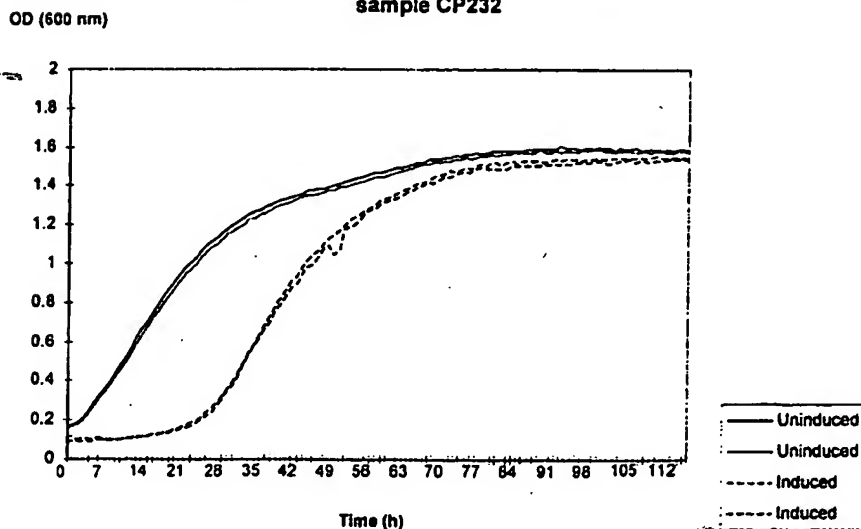


FIG. 32.

CP211-234+AF231-254 28/04/98  
 glucose/maltose vs galactose/maltose  
 sample CP232



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FIG. 33.

CP211-234+AF231-254 28/04/98  
glucose/maltose vs galactose/maltose  
sample CP233

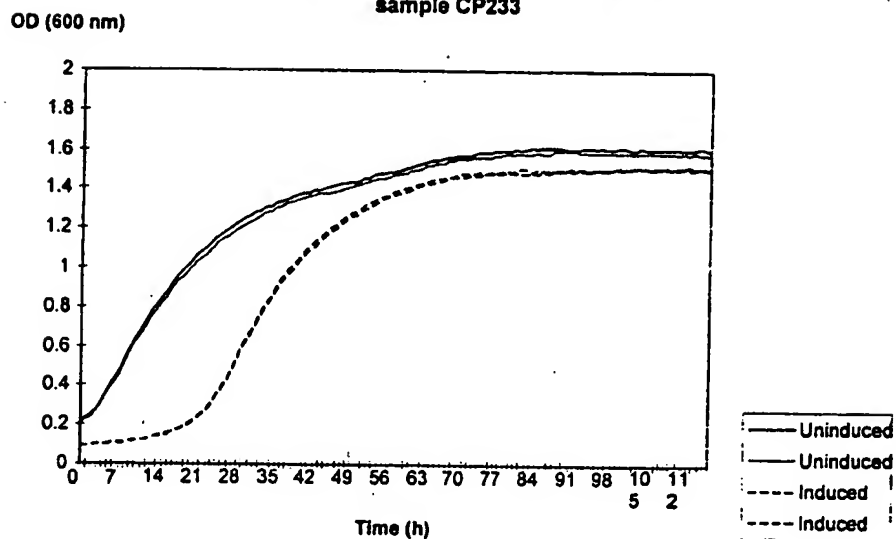
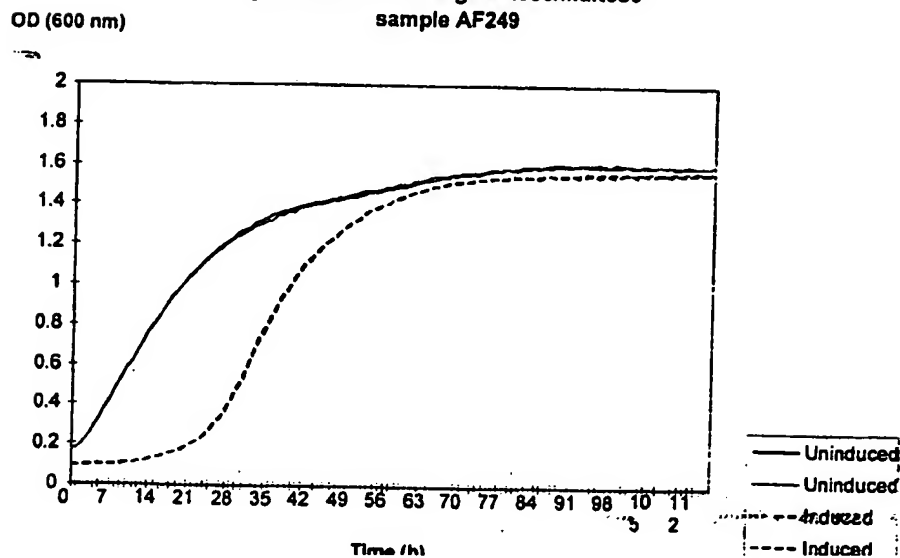


FIG. 34.

CP211-234+AF231-254 28/04/98 IVR  
glucose/maltose vs galactose/maltose  
sample AF249



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FIG. 35.

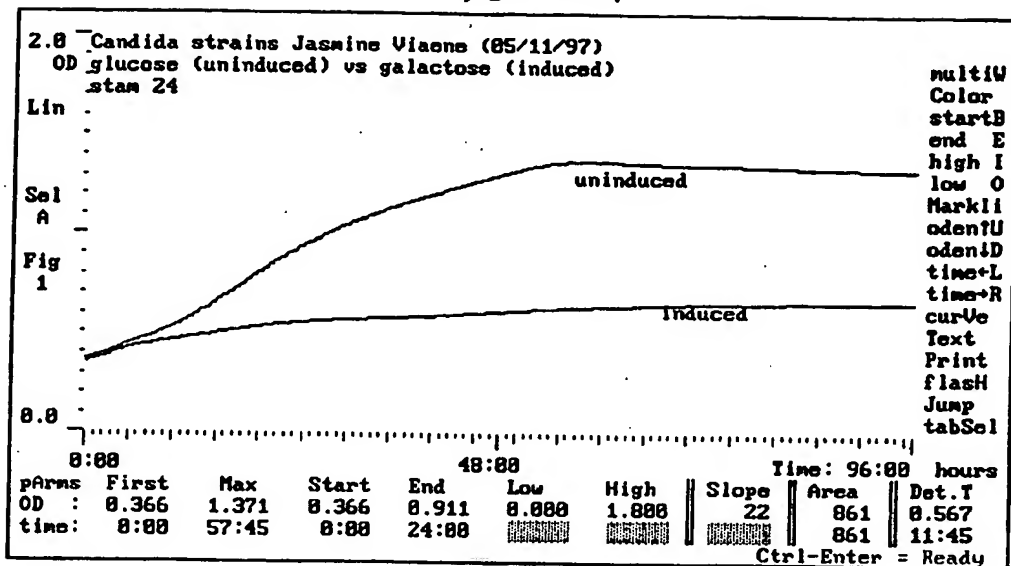
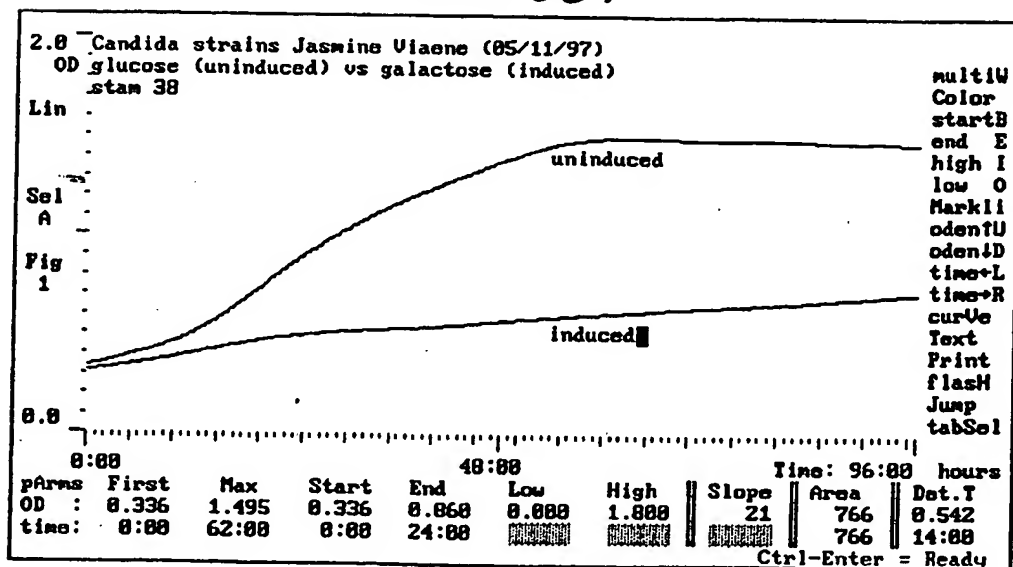


FIG. 36.



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FIG. 37

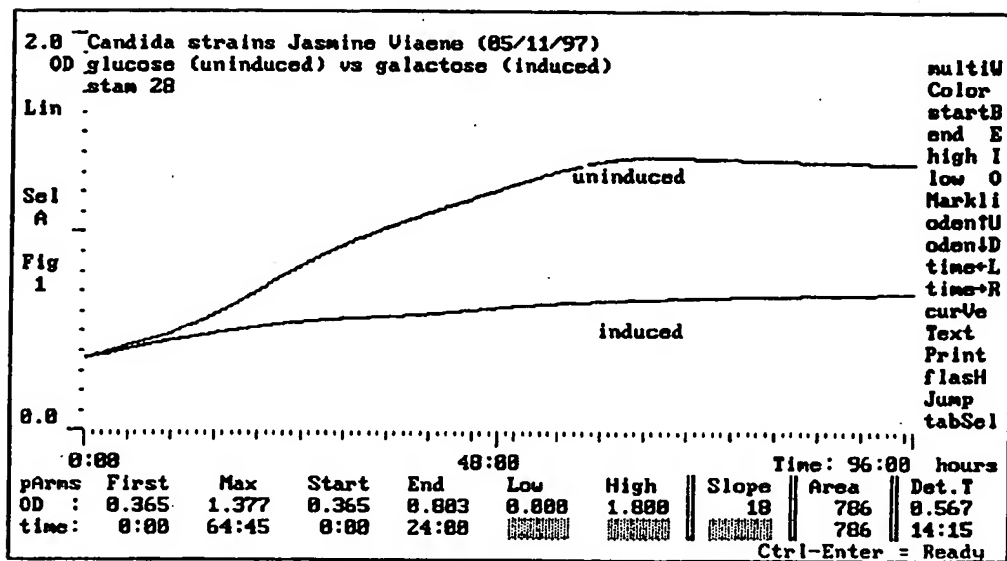
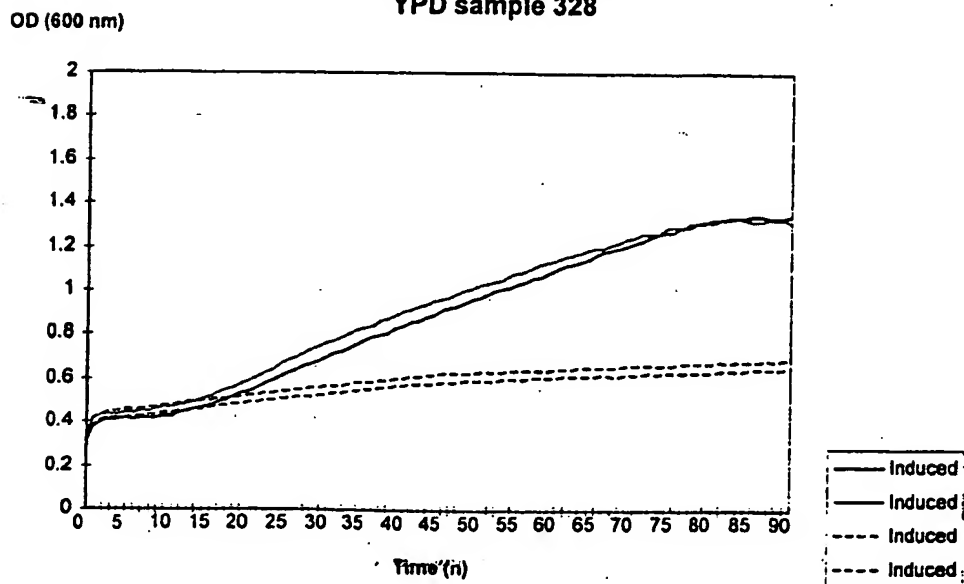


FIG. 38

C. albicans library screening experiment 27/10/97  
glucose vs galactose  
YPD sample 328





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FIG. 39

*C. albicans* cDNA library screening 12-02-98  
glucose/maltose vs galactose/maltose  
YPD sample 357

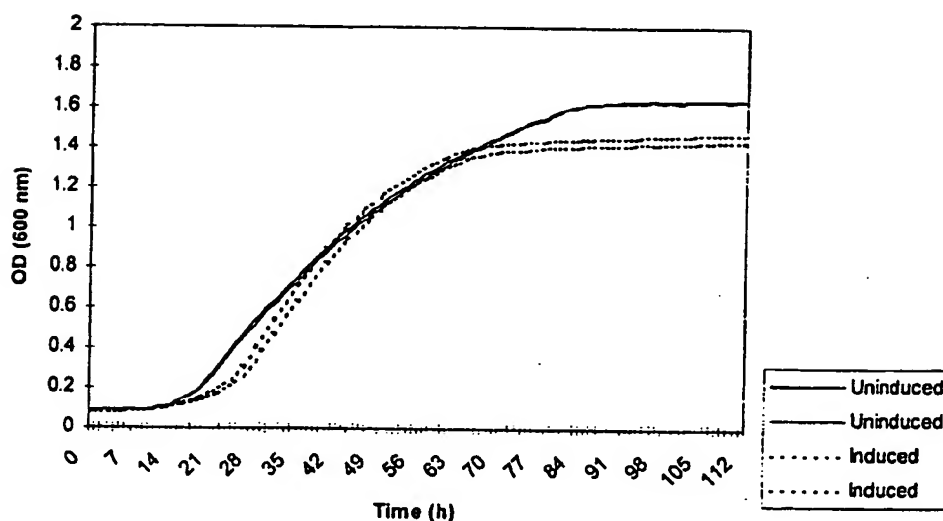
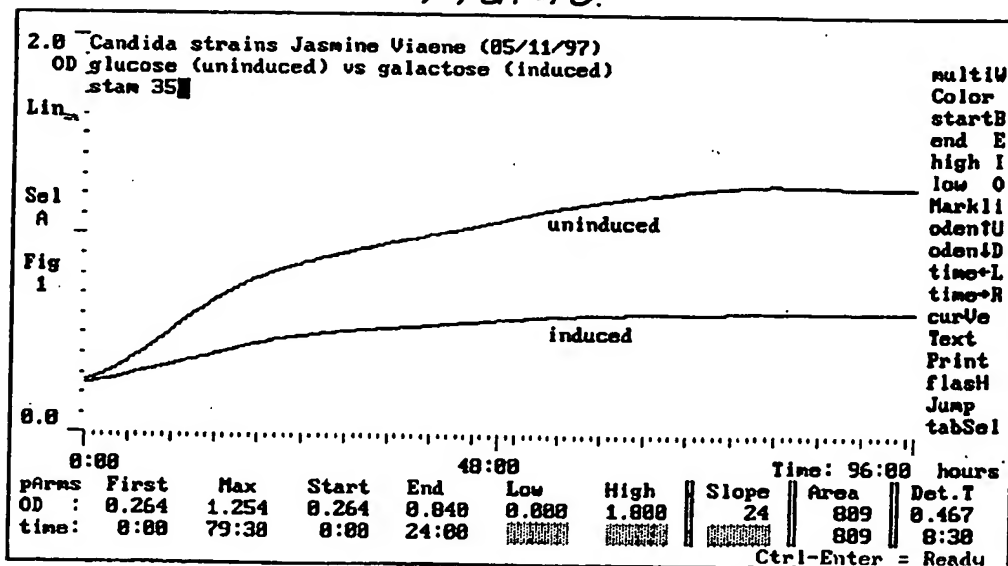


FIG. 40.



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FIG. 41.

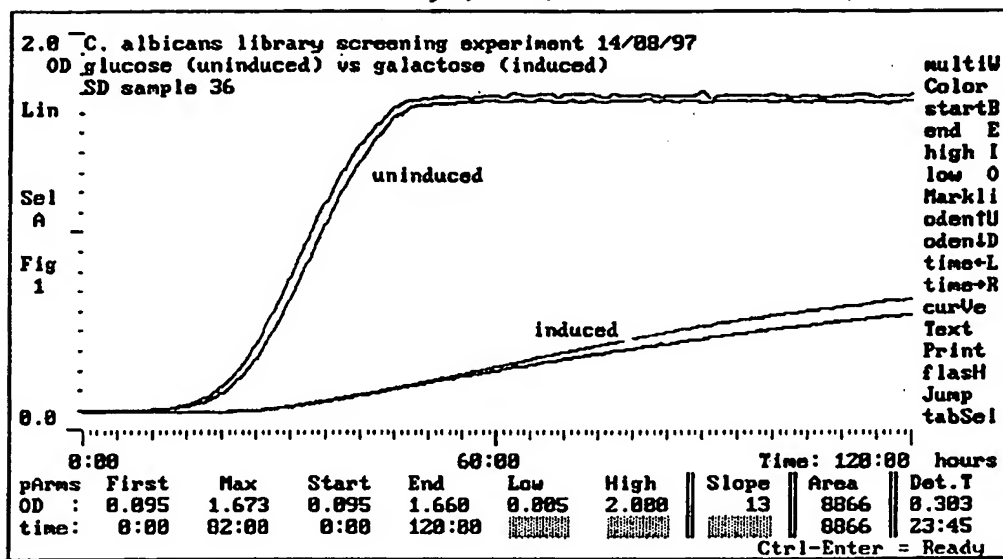
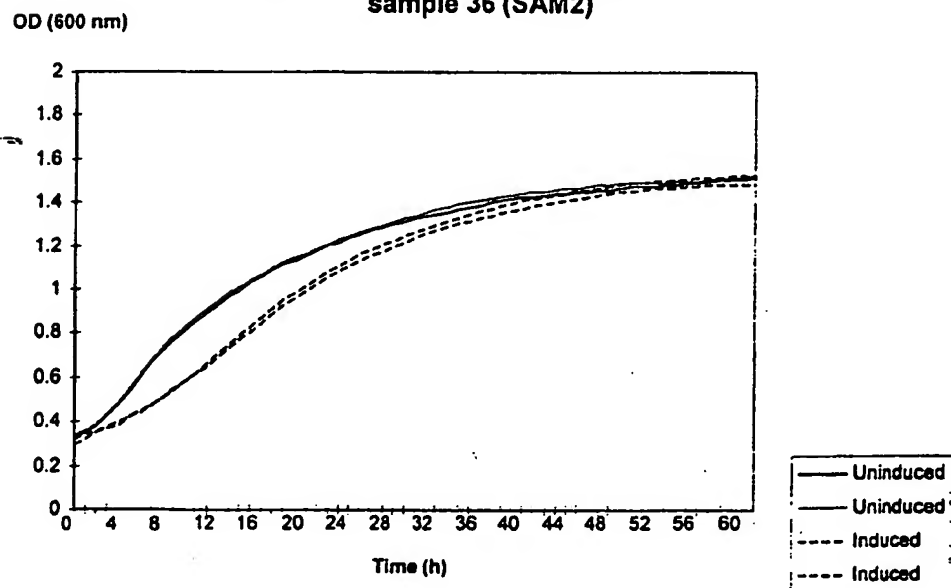


FIG. 42.

C. albicans library screening experiment 28/11/97  
glucose/maltose vs galactose/maltose  
sample 36 (SAM2)



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FIG. 43.

*C. albicans* cDNA library screening 05/02/98  
glucose/maltose vs galactose/maltose  
YPD sample 360

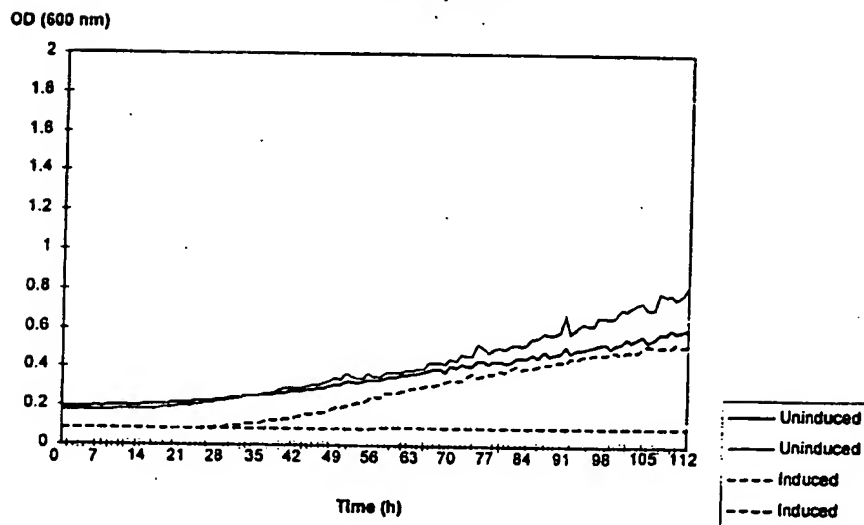
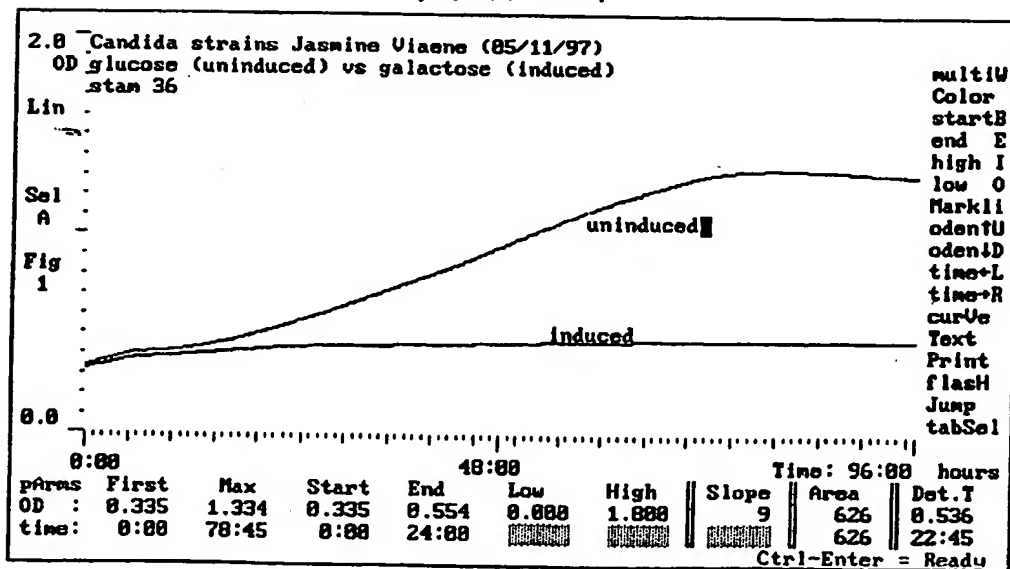


FIG. 44.



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FIG. 45.

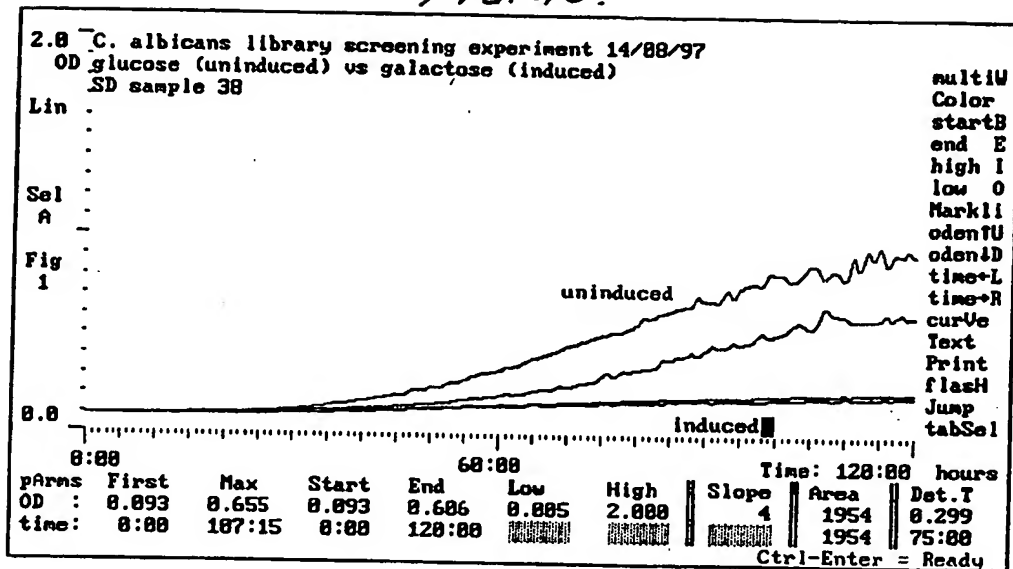
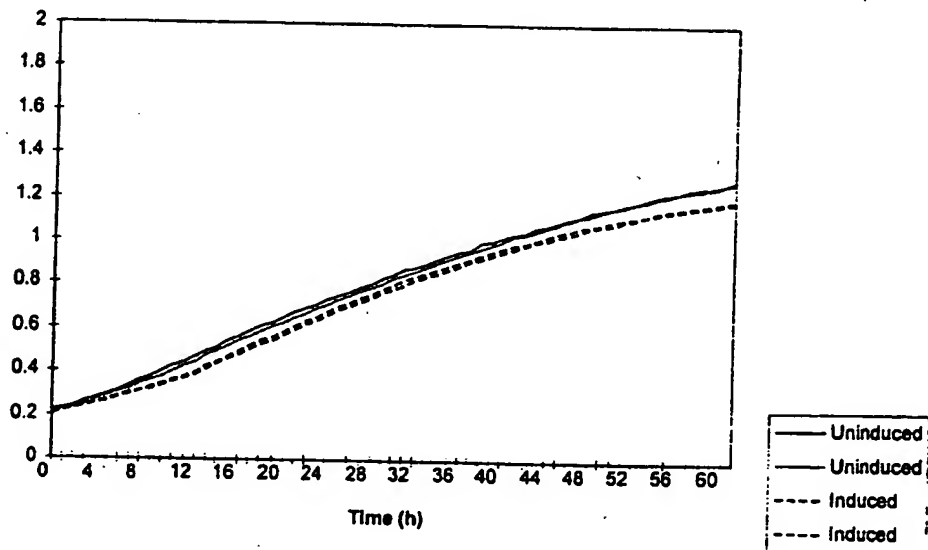


FIG. 46.

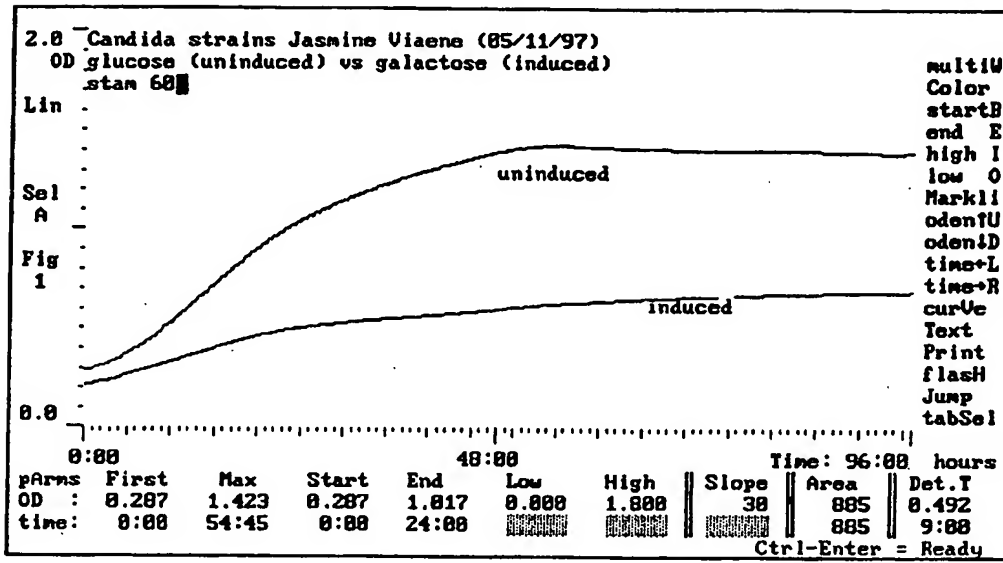
C. albicans library screening experiment 28/11/97  
glucose/maltose vs galactose/maltose  
sample 38 (RNR)

OD (600 nm)



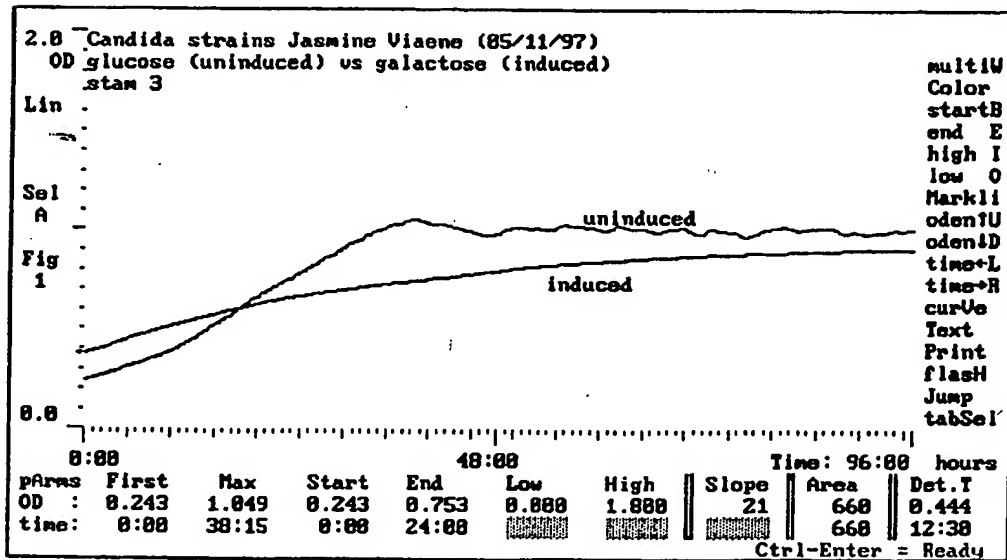
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FIG. 47.



60gK (RAD18)

FIG. 48.



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FIG. 49.

C. albicans cDNA library screening 12-02-98  
glucose/maltose vs galactose/maltose  
YPD sample 409

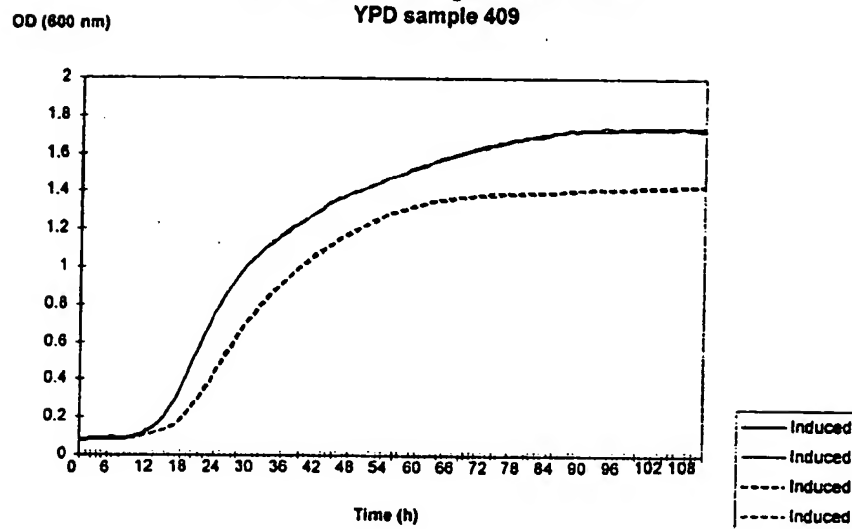
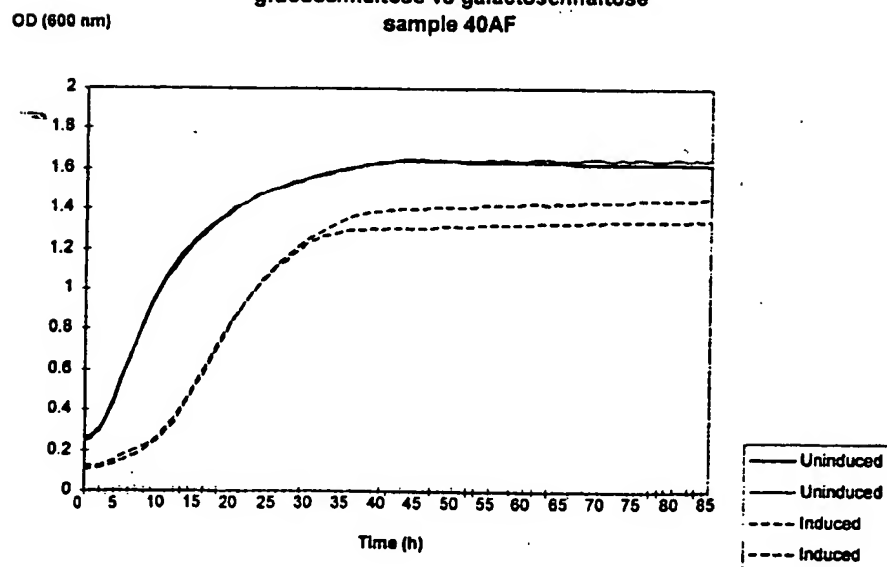


FIG. 50.

C. albicans library screening experiment 27/03/98  
glucose/maltose vs galactose/maltose  
sample 40AF



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FIG. 51.

C. albicans library screening experiment 17/03/98  
glucose/maltose vs galactose/maltose  
SD sample 485c

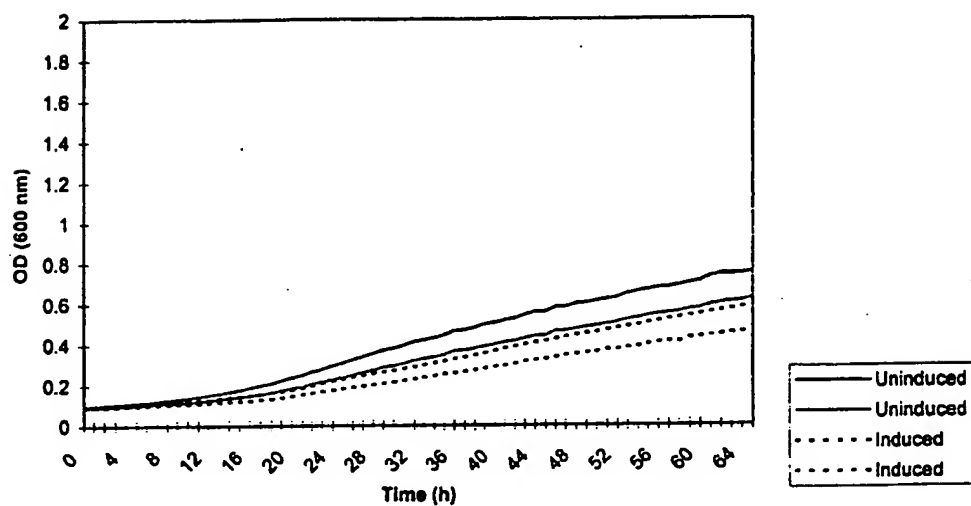
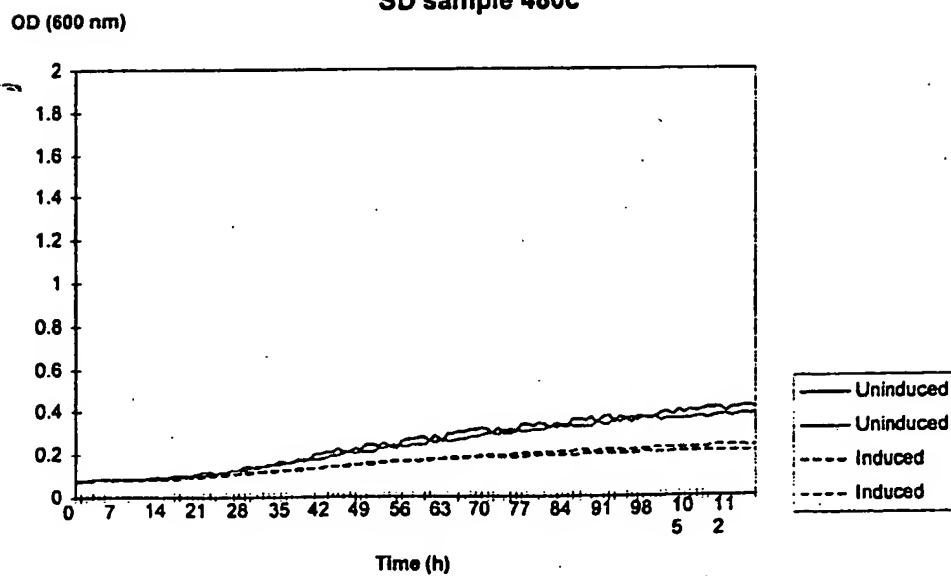


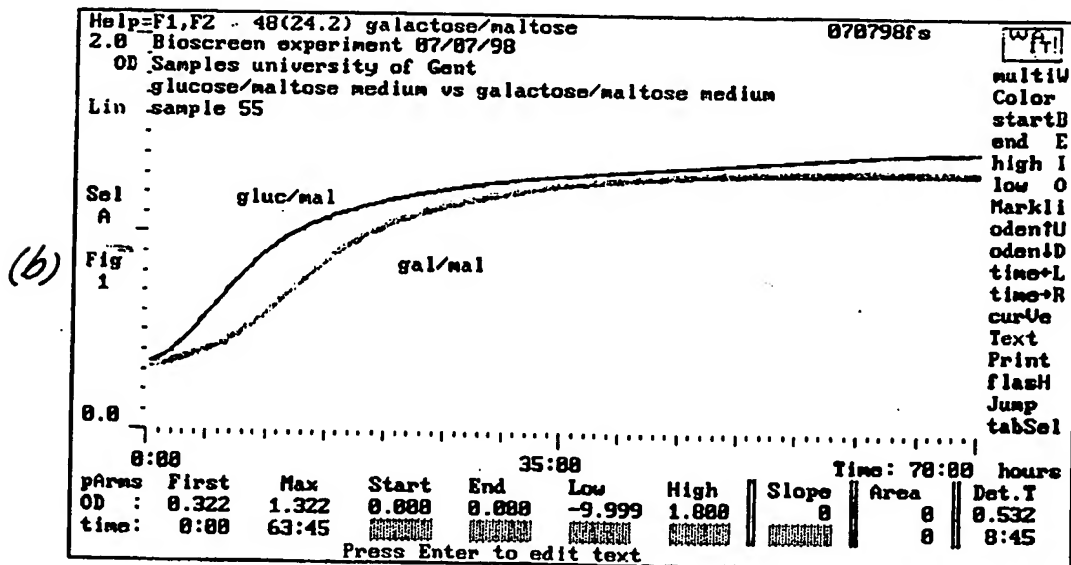
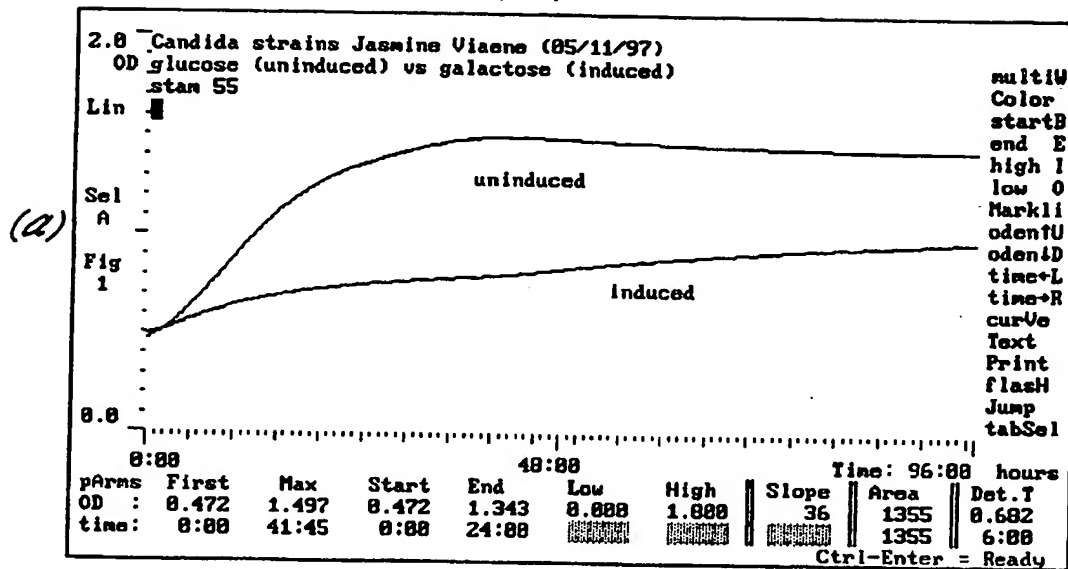
FIG. 52.

C. albicans cDNA library screening 10-03-98  
glucose vs galactose  
SD sample 480c



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FIG. 53.





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FIG. 54

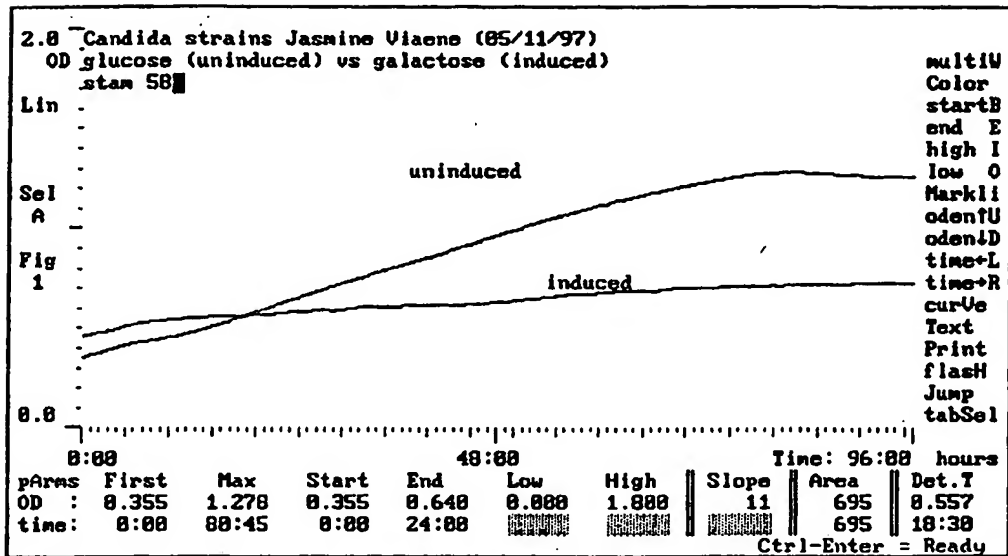
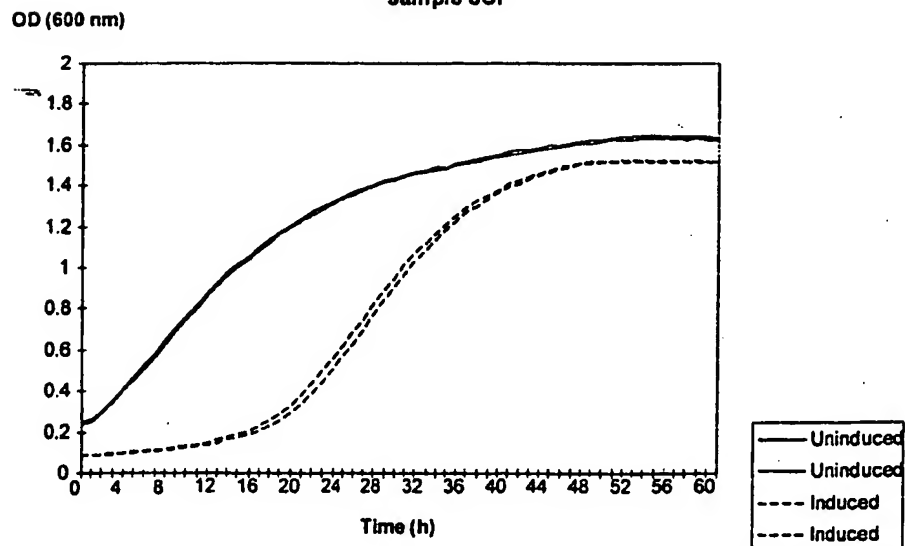


FIG. 55.

C. albicans library screening experiment 31/03/98  
 glucose/maltose vs galactose/maltose  
 sample 8CP



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FIG. 56.

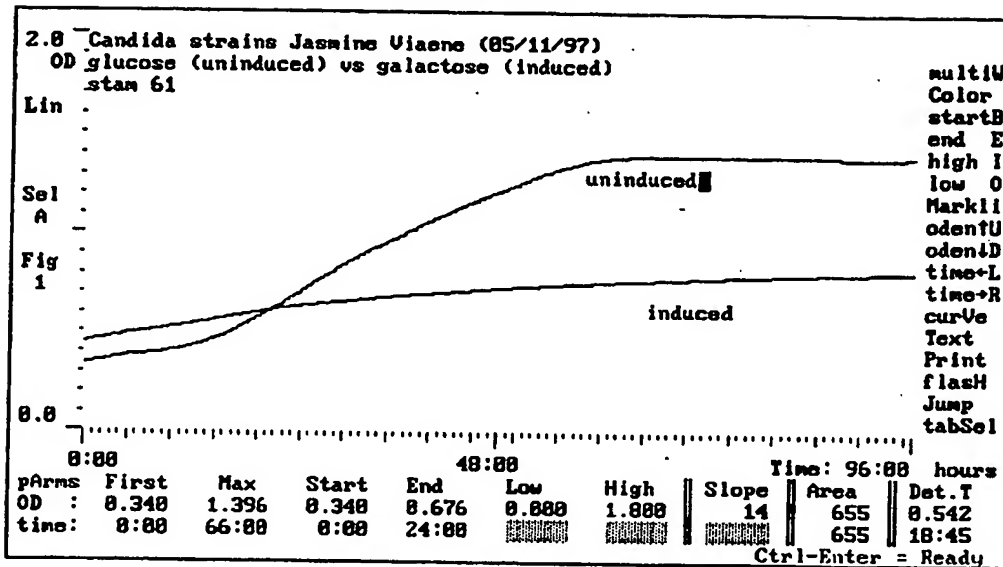
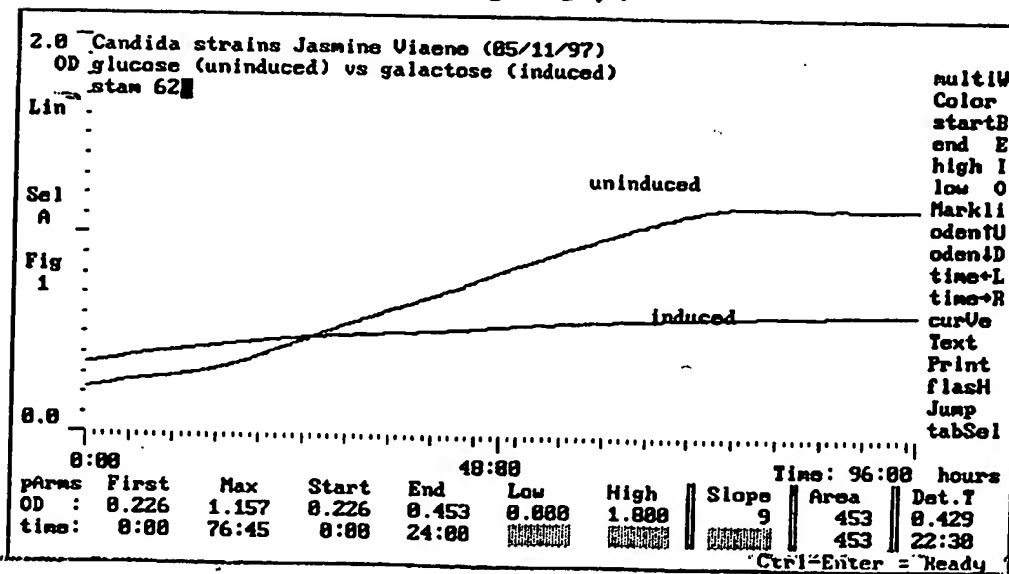


FIG. 57.



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FIG. 58.

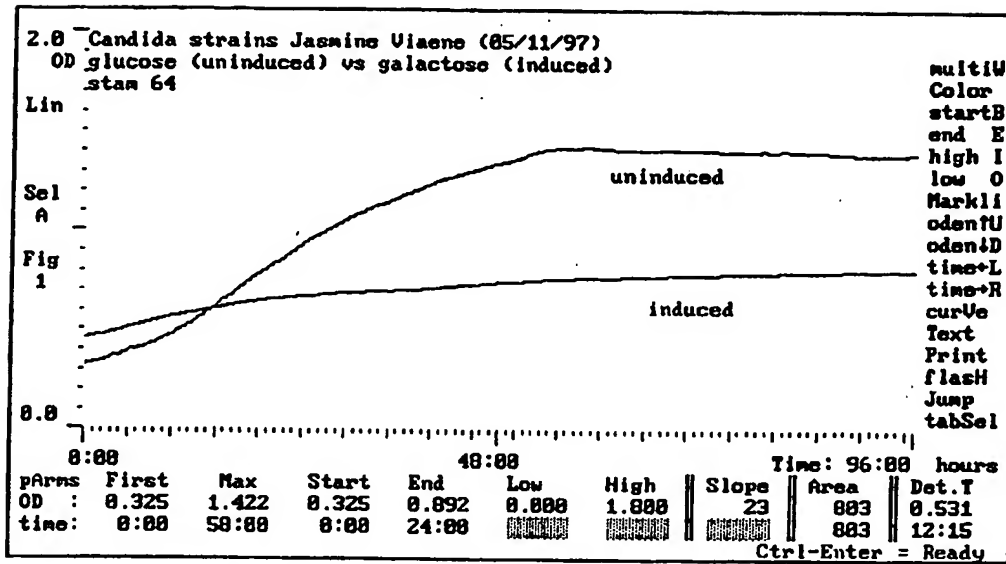
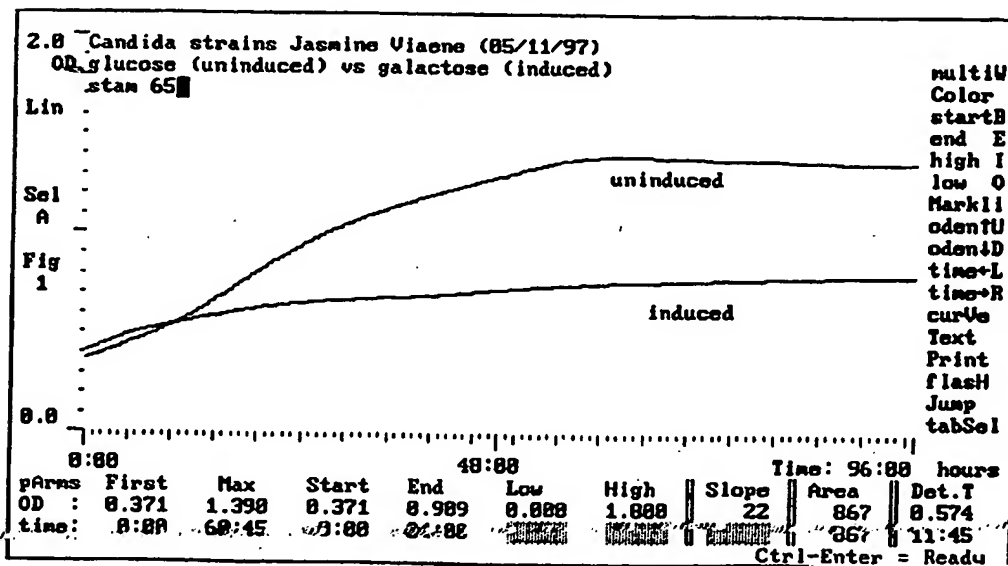


FIG. 59.



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FIG. 60.

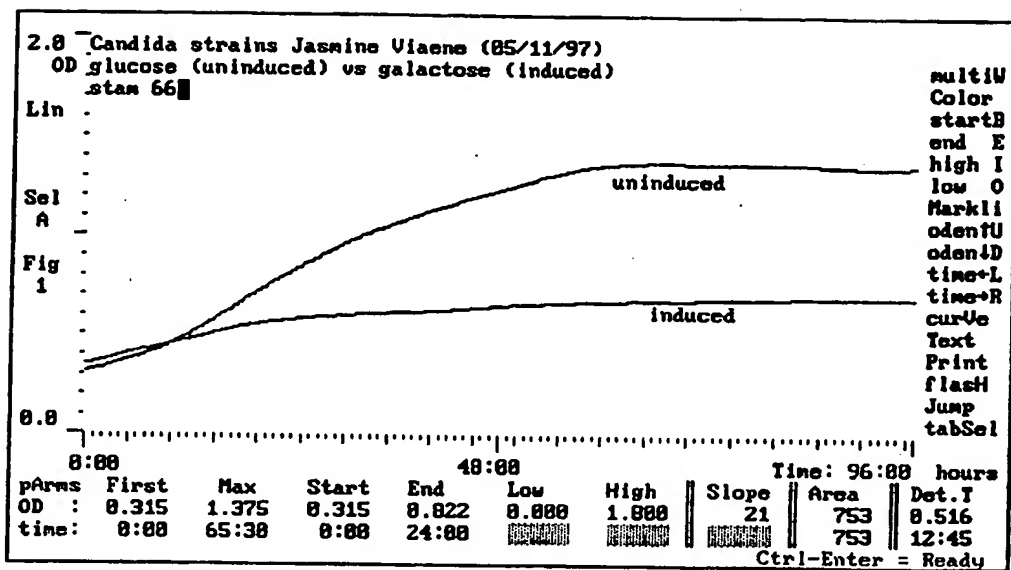
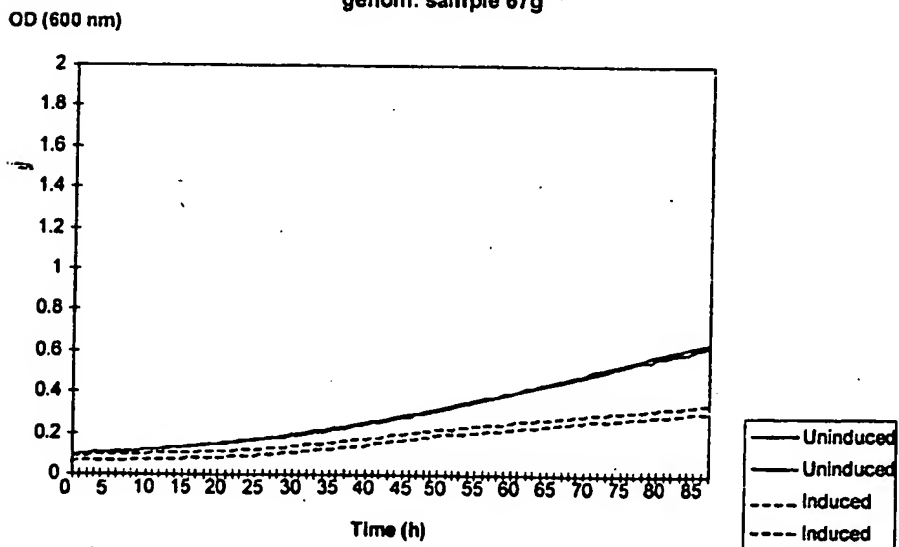


FIG. 61.

C. albicans library screening experiment 21/11/97  
 glucose vs galactose  
 genom. sample 67g



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FIG. 62.

*C. albicans* library screening experiment 21/11/97  
glucose vs galactose  
genom. sample 80g

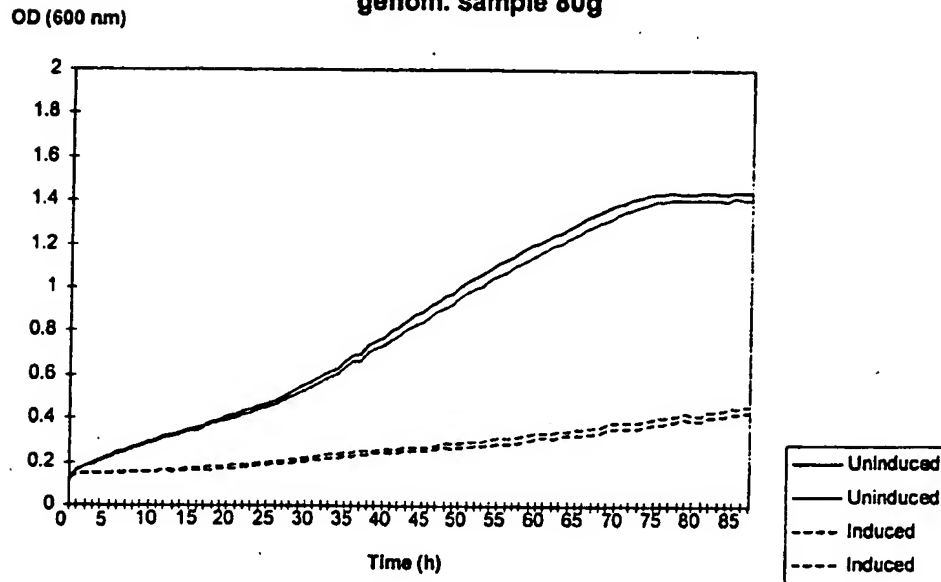
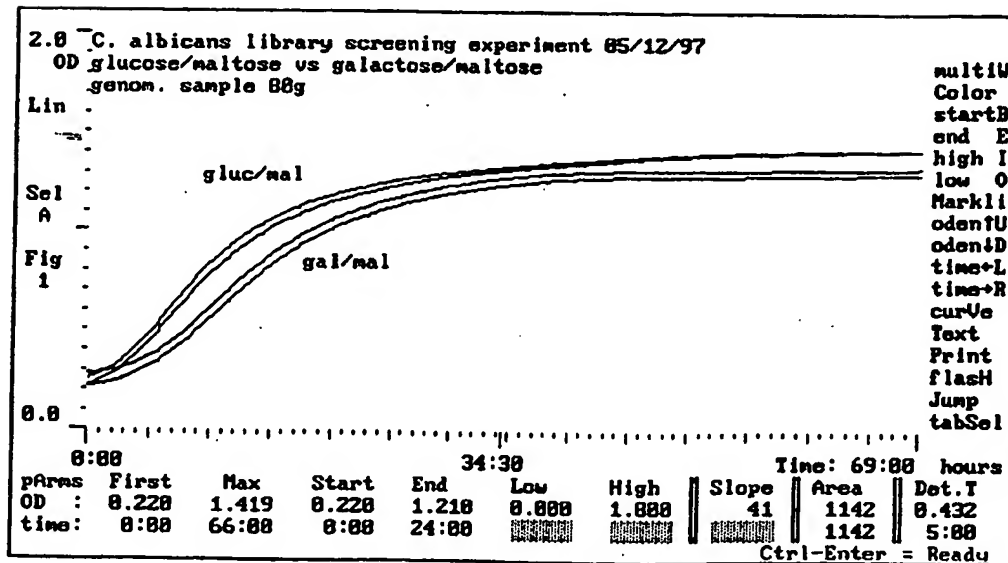


FIG. 63.





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FIG. 65.

C. albicans library screening experiment 21/11/97  
glucose vs galactose  
genom. sample 85g

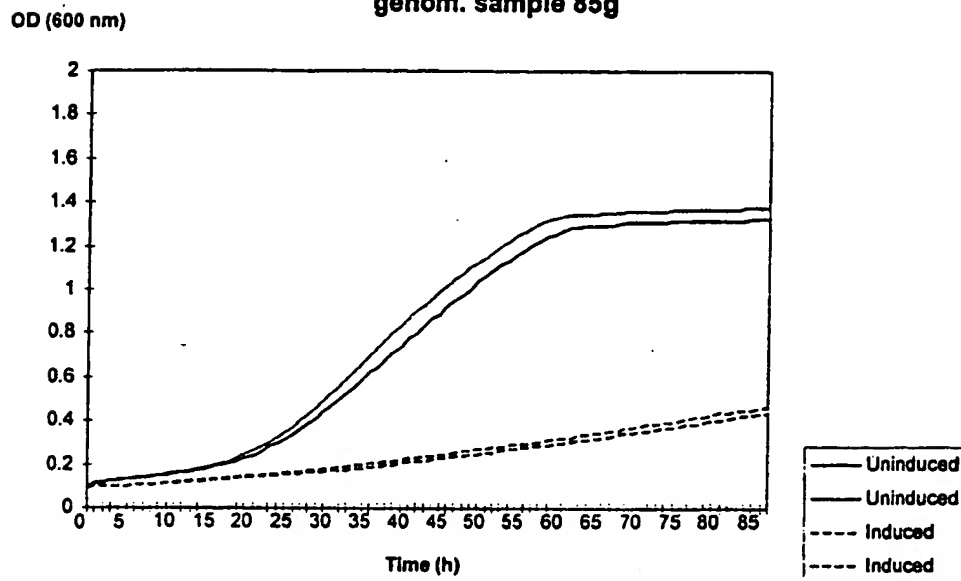
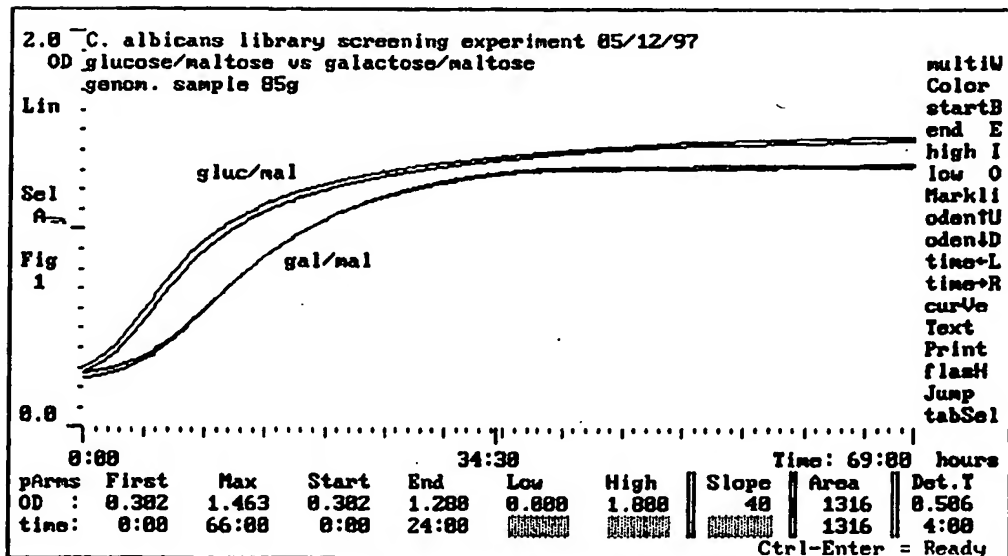


FIG. 66.



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FIG. 67.

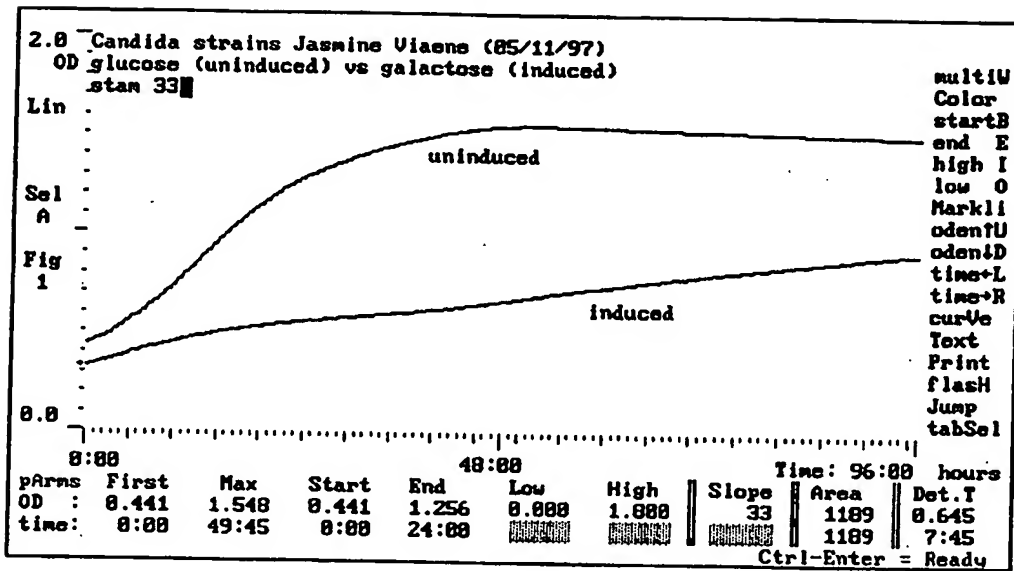
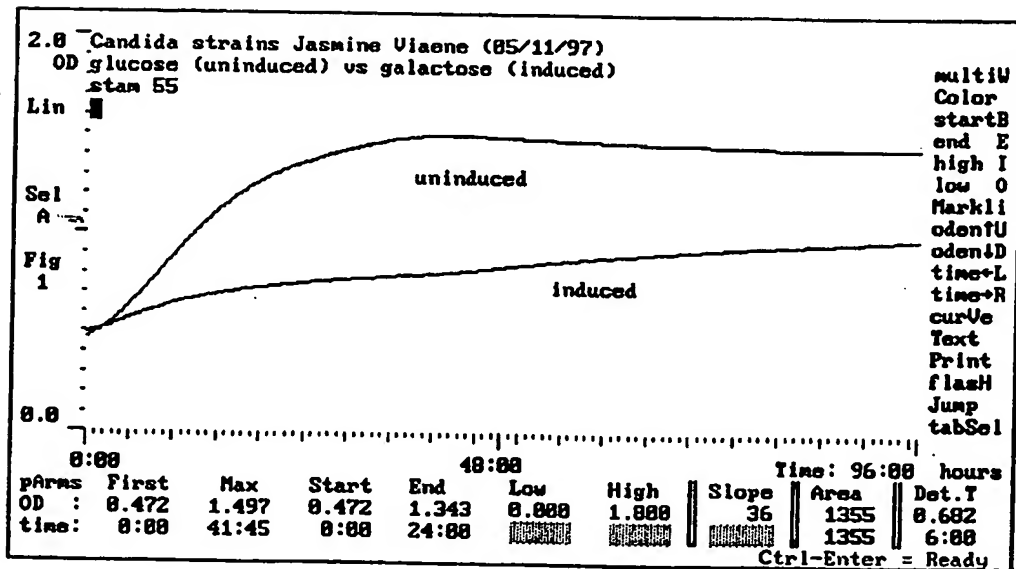


FIG. 68.





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FIG. 69.

C. albicans library screening experiment 21/11/97  
glucose vs galactose  
genom. sample 99g

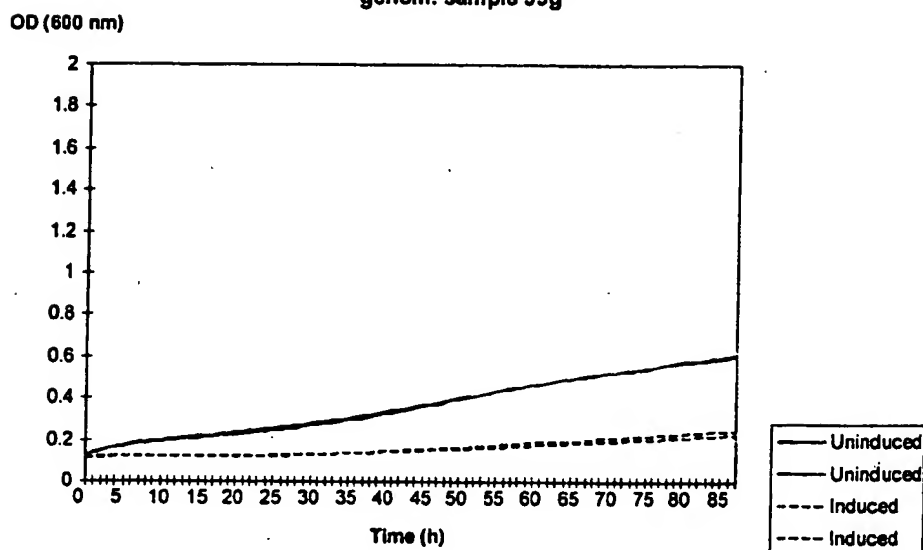
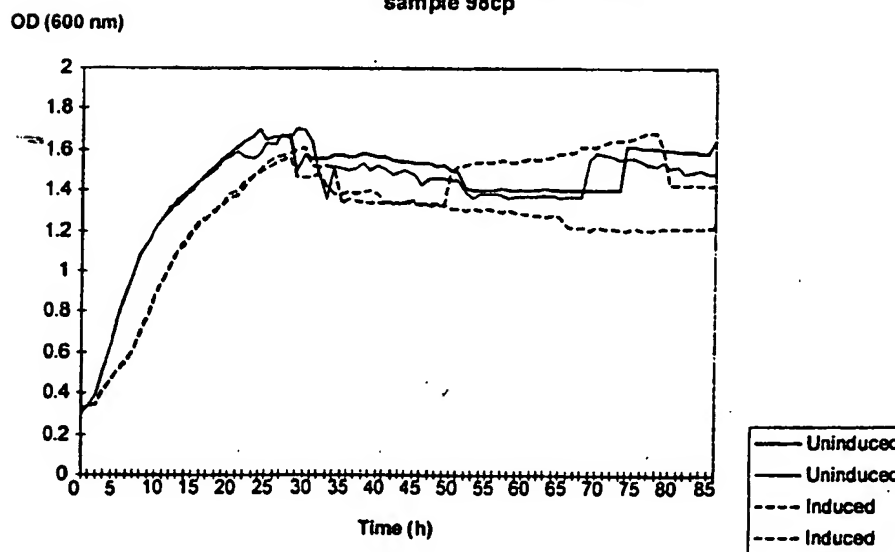


FIG. 70.

C. albicans library screening experiment 24/04/98  
glucose/maltose vs galactose/maltose  
sample 98cp



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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : <b>C12N 15/31, C07K 14/40, A61K 31/70, 38/16, C07K 16/14, G01N 33/50, C12Q 1/68</b>		A3	(11) International Publication Number: <b>WO 00/09695</b> (43) International Publication Date: <b>24 February 2000 (24.02.00)</b>
(21) International Application Number: <b>PCT/EP99/05991</b> (22) International Filing Date: <b>16 August 1999 (16.08.99)</b> (30) Priority Data: 9817796.7      14 August 1998 (14.08.98)      GB 98310694.9      23 December 1998 (23.12.98)      EP (71) Applicant (for all designated States except US): <b>JANSSEN PHARMACEUTICA N.V. [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE).</b> (72) Inventors; and (75) Inventors/Applicants (for US only): <b>CONTRERAS, Roland, Henri [BE/BE]; University of Gent, K.L. Ledeganckstraat 35, B-9000 Gent (BE). NELISSEN, Bart [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). DE BACKER, Marianne, Denise [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). LUYTEN, Walter, Herman, Maria, Louis [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). VIAENE, Jasmine, Elza [BE/BE]; University of Gent, K.L. Ledeganckstraat 35, B-9000 Gent (BE). LOGGHE, Marc, George [BE/BE]; University of Gent, K.L. Ledeganckstraat 35, B-9000 Gent (BE).</b>		(74) Agent: <b>BOULT WADE TENNANT; 27 Fumival Street, London EC4A 1PQ (GB).</b>  (81) Designated States: <b>AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</b>  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>  (88) Date of publication of the international search report: <b>22 June 2000 (22.06.00)</b>	
(54) Title: <b>DRUG TARGETS IN CANDIDA ALBICANS</b>			
(57) Abstract <p>The present invention is concerned with a method of identifying compounds which selectively modulate expression of polypeptides which are crucial for growth and survival of <i>Candida albicans</i>, which method comprises: (a) contacting a compound to be tested with one or more <i>Candida albicans</i> cells having a mutation in a nucleic acid molecule corresponding to the sequences according to any of claims 1 to 8 which mutation results in overexpression or underexpression of said polypeptides, in addition to contacting one or more wild type <i>Candida albicans</i> cells with said compound, (b) monitoring the growth and/or activity of said mutated cell compared to said wild type; wherein differential growth or activity of said one or more mutated <i>Candida</i> cells is indicative of selective action of said compound on a polypeptide or another polypeptide in the same or a parallel pathway. Also disclosed in the present invention are compounds identified and the sequences themselves which are critical for survival and growth of <i>Candida albicans</i>.</p>			

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 99/05991

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/31 C07K14/40 A61K31/70 A61K38/16 C07K16/14  
G01N33/50 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	REIFENBERGER E ET AL: "IDENTIFICATION OF NOVEL HXT GENES IN SACCHAROMYCES CEREVISIAE REVEALS THE IMPACT OF INDIVIDUAL HEXOSE TRANSPORTERS ON GLYCOLYTIC FLUX" MOLECULAR MICROBIOLOGY, GB, OXFORD, vol. 16, no. 1, 1 January 1995 (1995-01-01), pages 157-167, XP000572126	9, 10, 35
A	the whole document	23
A	EP 0 844 307 A (SMITHKLINE BEECHAM CORP) 27 May 1998 (1998-05-27) the whole document	24, 38, 39
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

1 February 2000

Date of mailing of the international search report

27.04.00

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Smart, R

# INTERNATIONAL SEARCH REPORT

Intern 1al Application No  
PCT/EP 99/05991

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DALY S ET AL: "Isolation and characterization of a gene encoding alpha-tubulin from Candida albicans" GENE: AN INTERNATIONAL JOURNAL ON GENES AND GENOMES,GB,ELSEVIER SCIENCE PUBLISHERS, BARKING, vol. 187, no. 2, 7 April 1997 (1997-04-07), page 151-158 XP004093273 ISSN: 0378-1119 the whole document</p> <p>---</p>	
A	<p>WO 97 36925 A (SCRIPTGEN PHARM INC ;HARVARD COLLEGE (US)) 9 October 1997 (1997-10-09) the whole document</p> <p>---</p>	
A	<p>WO 97 37230 A (BRADLEY JOHN;WOBBE C RICHARD; BURATOWSKI STEPHEN) 9 October 1997 (1997-10-09) the whole document</p> <p>---</p>	
A	<p>WO 96 36707 A (UNIV ROMA ;IST SUPERIORE SANITA (IT); CASSONE ANTONIO (IT); VALLE) 21 November 1996 (1996-11-21) the whole document</p> <p>-----</p>	

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 99/ 05991

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
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2. ☒ Claims Nos.: 25-28  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1,2,4-12,14-2°,34,35,38,39 all partially

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 25-28

Claims 25-28 refer to a compound identifiable with a method, without giving a true technical characterization of the compound. Moreover, no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 83 and 84 EPC). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Invention 1: claims 1,2,4-12,14-28,34,35,38,39,  
all partially

Nucleic acid molecule comprising seq.ID.1 or capable of hybridizing thereto, polypeptide of seq.ID.43 encoded by said nucleic acid, expression vector comprising said nucleic acid, antibody against said peptide, use of said vector for preparation of medicament or pharmaceutical composition, C. albicans cell comprising an induced mutation in said DNA sequence, oligonucleotides comprising 10-50 nt of said nucleic acid sequence, and method for identifying compounds which modulate expression of said nucleic acid.

2. Inventions 2-68: claims 1,6-11,15-28,34,35,38,  
39 partially, and 2-5,12-14,36,37,  
40 partially as applicable

As invention 1, but limited to the respective nucleic acid sequences 2,3,5,10,11,12,16,17,18,20,21,23,25,26,27,29,31, 33,35,37,39,41,44,45,46,49,50,52,55,57,59,61,63,65,67,70,72, 74,76,78,80,81,83,85,87,89,91,93,95,97,99,101,104,106,108,110 and 113, and polypeptide sequences corresponding to said nucleic acid sequences in as far as they are provided (see table 1 of the description), whereby invention 2 is limited to seq.ID.2, invention 3 is limited to seq.ID.3 and its translated polypeptide seq.ID.4, ....., and invention 68 is limited to seq.ID.113 and its translated polypeptide sequence seq.ID.114.

In as far as a polypeptide sequence, translated from the ORF of a corresponding nucleic acid sequence is provided, the polypeptide encoded by the corresponding nucleic acid sequence and their use in the preparation of a medicament, and antibodies against said polypeptide is also considered part of the respective invention.

3. Invention 69: claim 29-33

Method for identifying DNA sequences: from a cell or organism, which encode polypeptides which are critical for growth and survival for said cell or organism, comprising screening a library of nucleic acids using a vector that either integrates into the genome of said cell or organism, or that permits expression of antisense RNA, and selecting growth-impaired cells or organisms. Plasmids pGALIPSiST-1 and pGALIPNiST-1, used in said method.



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/05991

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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			CA 2216616 A	21-05-1998
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WO 9736925	A	09-10-1997	CA 2250129 A	09-10-1997
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## SEQUENCE LISTING

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<120> Drug Targets In Candida Albicans

<130> 50899/002

<140>

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<150> 98310694.9

<151> 1998-12-23

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Lys Thr Met Val Leu Thr Glu Ile Lys Thr Ile Thr Glu Phe Ala Thr  
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&lt;212&gt; PRT

&lt;213&gt; Candida albicans

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Gln Ile Phe Ser Val Val Pro Ala Ser Gly Asn Leu Thr His Gln Pro  
 35 40 45

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 50 55 60

Val Thr His Val Phe Phe Val Gln Gly Trp Trp Tyr Tyr  
 65 70 75

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 <213> Candida albicans

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 tttgcaatca ccctgactcg tttttttttc agccagtttt ttcgtaaaat ctgacaaaaa 240  
 atttacaact ctaattttaa actctaaata acaattaaaa ctcaattcag acaagtcctt 300  
 ctgctcatte tgagtcttct ctattgtctt ttgacttttt gtgtgtgact attttcatga 360  
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<210> 11  
 <211> 582  
 <212> DNA  
 <213> Candida albicans

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 ccaaataaac tttagactca caactcctaac actgactcgt gccccctgt ttaaactcta 240  
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 ctcatcttga gtcttctcta ttgtcttttg actttttgtg tgtgactatt ttcgatgaca 480  
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<210> 12

<211> 1066

<212> DNA

<213> Candida albicans

<400> 12

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<210> 13

<211> 302

<212> PRT

<213> Candida albicans

<400> 13

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Gly	Asn	Pro	Val	Ala	Val	Ile	Tyr	Asp	Ser	Asp	Asn	Leu	Thr	Thr	Gln
			20						25					30	
Glu	Met	Gln	Lys	Ile	Ala	Arg	Trp	Thr	Asn	Leu	Ser	Glu	Thr	Thr	Phe

35                                      40                                      45  
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     50                                      55                                      60  
 Thr Ser Gly Gly Asn Glu Leu Pro Phe Ala Gly His Pro Thr Leu Gly  
     65                                      70                                      75                                      80  
 Thr Ala Phe Ala Leu Leu Glu Asp Gly Lys Ile Lys Pro Asn Asp Asn  
                                     85                                      90                                      95  
 Gly Gln Ile Ile Gln Glu Cys Gly Ala Gly Leu Val Lys Ile Ser Val  
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 Glu Lys Thr Pro Asn Asn Asn Ser Asn Glu Leu Pro Phe Leu Leu Ser  
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 Val Leu Ile Asp Ala Gly Pro Lys Trp Ala Val Phe Gln Leu Gly Ser  
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 Gly Lys Glu Val Leu Asp Leu Asn Xaa Asp Leu Ala Gln Ile Glu Arg  
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 Asn Glu Asn Gly Asp Ser Val Glu Leu Arg Asn Ile Ala Pro Ala Val  
                                     210                                      215                                      220  
 Gly Val Ala Glu Asp Pro Ala Cys Gly Ser Gly Ser Gly Ala Ile Gly  
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 Ala Tyr Leu Ala Asn His Val Phe Asn Glu Lys Glu Lys Phe Thr Ile  
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 Asp Ile Ser Gln Gly Lys Pro Ile Glu Arg Asp Ala Lys Ile Gln Val  
                                     260                                      265                                      270  
 Lys Val Asn Arg Leu Thr Thr Lys Asn Gly Asp Leu Ser Ile His Val  
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 Gly Gly His Ala Ile Thr Cys Phe Glu Gly Thr Tyr Ser Ile

290

295

300

&lt;210&gt; 14

&lt;211&gt; 3726

&lt;212&gt; DNA

<213> *Candida albicans*

&lt;400&gt; 14

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 cctaaa 3726

&lt;210&gt; 15

&lt;211&gt; 942

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 15

Met Thr Glu Thr Val Ile Glu Lys Lys Arg Lys Val Asp Leu Asn Ala  
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Ser Gly Ile Thr Lys Gln Pro Lys Ala Ser Lys Ile Phe Ser Pro Phe  
 20 25 30

Arg Val Leu Gly Asn Val Thr Asp Ser Thr Pro Phe Ala Met Gly Thr  
 35 40 45

Leu Gly Ser Thr Phe Tyr Ala Val Thr Ser Val Gly Arg Ser Phe Gln  
 50 55 60

Ile Tyr Asp Leu Ala Thr Leu His Leu Leu Phe Val Ser Gln Thr Gln  
 65 70 75 80

Thr Pro Ser Arg Ile Thr Ser Leu Ala Ala His His His Tyr Val Tyr  
 85 90 95

Ala Ser Tyr Gly Asp Arg Ile Gly Ile Phe Arg Arg Gly Arg Leu Glu  
 100 105 110  
 His Glu Leu Val Cys Glu Gly Asn Ser Thr Val Asn Gln Leu Leu Val  
 115 120 125  
 Phe Gly Glu Tyr Leu Ile Ala Thr Thr Leu Glu Gly Asp Ile Phe Val  
 130 135 140  
 Phe Arg Lys Thr Glu Gly Lys Lys Phe Pro Thr Glu Leu Tyr Thr Thr  
 145 150 155 160  
 Ile Arg Ile Ile Asn Ser Leu Val Glu Gly Glu Ile Val Gly Leu Ile  
 165 170 175  
 His Pro Pro Thr Tyr Leu Asn Lys Val Ile Val Ala Thr Thr Gln Ser  
 180 185 190  
 Val Phe Val Ile Asn Val Arg Thr Gly Lys Leu Leu Tyr Lys Ser Arg  
 195 200 205  
 Glu Leu Gln Phe Glu Gly Glu Lys Ile Ser Ser Ile Glu Ala Ala Pro  
 210 215 220  
 Val Leu Asp Val Ile Ala Val Gly Thr Ser Asn Gly Asn Val Phe Leu  
 225 230 235 240  
 Phe Asn Ile Lys Lys Gly Lys Val Leu Gly Gln Lys Ile Ile Thr Ser  
 245 250 255  
 Gly Thr Glu Ser Ser Ser Lys Val Ala Ser Ile Ser Phe Arg Thr Asp  
 260 265 270  
 Gly Ala Pro His Leu Val Ala Gly Leu Asn Asn Gly Asp Leu Tyr Phe  
 275 280 285  
 Tyr Asp Leu Asp Lys Lys Ser Arg Val His Val Leu Arg Asn Ala His  
 290 295 300  
 Lys Glu Thr His Gly Gly Val Ala Asn Ala Lys Phe Leu Asn Gly Gln  
 305 310 315 320  
 Pro Ile Val Leu Ser Asn Gly Gly Asp Asn His Leu Lys Glu Phe Val  
 325 330 335  
 Phe Asp Pro Asn Leu Thr Thr Ser Asn Ser Ser Ile Val Pro Pro Pro  
 340 345 350



Arg His Leu Arg Ser Arg Gly Gly His Ser Ala Pro Pro Val Ala Ile  
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 Glu Phe Pro Gln Glu Asp Lys Thr His Phe Leu Leu Ser Ala Ser Arg  
 370 375 380  
 Asp Lys Thr Phe Trp Ile Phe Ser Leu Arg Lys Asp Ala Gln Ala Gln  
 385 390 395 400  
 Glu Met Ser Gln Arg Leu Gln Lys Ser Lys Asp Gly Lys Arg Gln Ala  
 405 410 415  
 Gly Gln Val Val Ser Met Arg Glu Lys Phe Pro Glu Ile Ile Ser Ile  
 420 425 430  
 Ser Ser Ser Tyr Ala Arg Glu Gly Asp Trp Glu Asn Ile Ile Thr Ala  
 435 440 445  
 His Lys Asp Glu Thr Phe Ala Arg Thr Trp Asp Ser Arg Asn Lys Arg  
 450 455 460  
 Val Gly Arg His Leu Leu Asn Thr Ile Asp Gly Gly Ile Val Lys Ser  
 465 470 475 480  
 Val Cys Val Ser Gln Cys Gly Asn Phe Gly Leu Val Gly Ser Ser Ser  
 485 490 495  
 Gly Gly Ile Gly Ser Tyr Asn Leu Gln Ser Gly Leu Leu Arg Lys Lys  
 500 505 510  
 Tyr Val Leu His Lys Gln Ala Val Thr Gly Leu Ala Ile Asp Gly Met  
 515 520 525  
 Asn Arg Lys Met Val Ser Cys Gly Leu Asp Gly Ile Val Gly Phe Tyr  
 530 535 540  
 Asp Phe Gly Lys Ser Val Tyr Leu Gly Lys Leu Gln Leu Glu Ala Pro  
 545 550 555 560  
 Ile Thr Ser Met Ile Tyr His Lys Ser Ser Asp Leu Val Ala Cys Ala  
 565 570 575  
 Leu Asp Asp Leu Ser Ile Val Val Ile Asp Val Thr Thr Gln Lys Val  
 580 585 590  
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 595 600 605

Ser Pro Asp Gly Arg Trp Ile Val Ser Val Ala Leu Asp Ser Thr Leu  
 610 615 620

Arg Thr Trp Asp Leu Pro Thr Gly Gly Cys Ile Asp Gly Val Ile Leu  
 625 630 635 640

Pro Ile Val Ala Thr Ala Val Lys Phe Ser Pro Ile Gly Asp Ile Leu  
 645 650 655

Ala Thr Thr His Val Ser Gly Asn Gly Val Ser Leu Trp Thr Asn Arg  
 660 665 670

Ala Gln Phe Lys Pro Val Ser Thr Arg His Val Glu Glu Asp Glu Phe  
 675 680 685

Ser Thr Ile Leu Leu Pro Asn Ala Ser Gly Asp Gly Gly Ser Thr Met  
 690 695 700

Leu Asp Gly Phe Leu Asp Glu Asp Ser Asn Glu Asp Gly Thr Ile Asp  
 705 710 715 720

Glu Gln Tyr Thr Ser Ala Ala Gln Ile Asp Ala Ser Leu Ile Thr Leu  
 725 730 735

Ser Ser Glu Pro Arg Ser Lys Phe Asn Thr Leu Leu His Leu Asp Thr  
 740 745 750

Ile Lys Gln Gln Ser Lys Pro Lys Glu Ala Pro Lys Lys Pro Glu Asn  
 755 760 765

Ala Pro Phe Phe Leu Gln Leu Thr Gly Gln Ala Val Gly Asp Arg Ala  
 770 775 780

Ser Val Ala Glu Gly Lys Thr Ser Glu Gln Thr Asn Asn Thr Val Glu  
 785 790 795 800

Glu Thr Asn Ser Lys Leu Arg Lys Leu Asp Thr Asn Gly Asn His Ala  
 805 810 815

Phe Glu Ser Glu Phe Thr Lys Leu Leu Arg Glu Ala Gly Glu Ser Gly  
 820 825 830

Gln Phe Glu Arg Phe Leu Thr Tyr Leu Leu Asn Leu Ser Pro Ala Val  
 835 840 845

Leu Asp Leu Glu Ile Arg Ser Leu Asn Ser Phe Val Pro Leu Thr Glu  
 850 855 860

Met Thr Asn Phe Ile Gln Ala Leu Asn Ala Gly Leu Lys Ser Asn Ala  
865 870 875 880

Asn Tyr Glu Ile Trp Glu Thr Leu Tyr Ala Met Phe Phe Asn Ile His  
885 890 895

Gly Asp Val Ile His Gln Phe Glu Asn Glu Thr Ser Leu His Glu Ala  
900 905 910

Leu Glu Glu Tyr Arg Gln Leu Asn Asp Glu Lys Asn Asn Lys Met Asp  
915 920 925

Ser Leu Val Lys Tyr Cys Ala Ser Ile Val Ser Phe Ile Ser  
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<211> 725

<212> DNA

<213> Candida albicans

<400> 16

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aagtaattta gagtttaaac aggggggcac gagtcagtgt tagagttgtg aagtttattt 660  
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aggtt 725

<210> 17

<211> 626

<212> DNA

<213> Candida albicans

<400> 17

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 ggaaatcaag cctctgaaat gaatcacaat ataataacaa tttgtagttg cagagaaaaa 540  
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<210> 18

<211> 667

<212> DNA

<213> Candida albicans

<400> 18

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 tttttcataa ttaataacta tcattactta caactacaaa caactacgat catttcctaa 600  
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 acagaac 667

<210> 19

<211> 5

<212> PRT

<213> Candida albicans

<400> 19

Met Pro Tyr Thr Glu

1

5

<210> 20

<211> 165

<212> DNA

<213> Candida albicans

<400> 20

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<210> 21

<211> 564

&lt;212&gt; DNA

<213> *Candida albicans*

&lt;400&gt; 21

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ttaccacttt attcgtgcat tatt                                     564

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&lt;210&gt; 22

&lt;211&gt; 136

&lt;212&gt; PRT

<213> *Candida albicans*

&lt;400&gt; 22

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Arg Tyr Ala Gly Lys Lys Val Val Ile Val Lys Pro His Asp Glu Gly
          20           25           30

Thr Lys Ser His Pro Phe Pro His Ala Ile Val Ala Gly Ile Glu Arg
      35           40           45

Ala Pro Leu Lys Val Thr Lys Lys Met Asp Ala Lys Lys Val Thr Lys
      50           55           60

Arg Thr Lys Val Lys Pro Phe Val Lys Leu Val Asn Tyr Asn His Leu
      65           70           75           80

Met Pro Thr Arg Tyr Ser Leu Asp Val Glu Ser Phe Lys Ser Ala Val
          85           90           95

Thr Ser Glu Ala Leu Glu Glu Pro Ser Gln Arg Glu Glu Ala Lys Lys
      100           105           110

Val Val Lys Lys Ala Phe Glu Glu Lys His Gln Ala Gly Lys Asn Lys
      115           120           125

Trp Phe Phe Gln Lys Leu His Phe
      130           135

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 <211> 1192  
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 <213> *Candida albicans*

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 <212> PRT  
 <213> *Candida albicans*

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 Gln Leu Leu Leu Lys Val Asp Ala Val Gly Leu Cys His Ser Asp Leu  
 35 40 45  
 His Val Leu Tyr Glu Gly Leu Asp Cys Gly Asp Asn Tyr Val Met Gly  
 50 55 60  
 His Glu Ile Ala Gly Thr Val Ala Glu Leu Gly Glu Glu Val Ser Glu  
 65 70 75 80

Phe Ala Val Gly Asp Arg Val Ala Cys Val Gly Pro Asn Gly Cys Gly  
                             85                            90                            95

Leu Cys Lys His Cys Leu Thr Gly Asn Asp Asn Val Cys Thr Lys Ser  
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Phe Leu Asp Trp Phe Gly Leu Gly Tyr Asn Gly Gly Tyr Glu Gln Phe  
                             115                            120                            125

Leu Leu Val Lys Arg Pro Arg Asn Leu Val Lys Ile Pro Asp Asn Val  
                             130                            135                            140

Thr Ser Glu Glu Ala Ala Ala Ile Thr Asp Ala Val Leu Thr Pro Tyr  
                             145                            150                            155                            160

His Ala Ile Lys Ser Ala Gly Val Gly Pro Ala Ser Asn Ile Leu Ile  
                             165                            170                            175

Ile Gly Ala Gly Gly Leu Gly Gly Asn Ala Ile Gln Val Ala Lys Ala  
                             180                            185                            190

Phe Gly Ala Lys Val Thr Val Leu Asp Lys Lys Asp Lys Ala Arg Asp  
                             195                            200                            205

Gln Ala Lys Ala Phe Gly Ala Asp Gln Val Tyr Ser Glu Leu Pro Asp  
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Ser Val Leu Pro Gly Ser Phe Ser Ala Cys Phe Asp Phe Val Ser Val  
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Gln Ala Thr Tyr Asp Leu Cys Gln Lys Tyr Cys Glu Pro Lys Gly Thr  
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Ile Val Pro Val Gly Leu Gly Ala Thr Ser Leu Asn Ile Asn Leu Ala  
                             260                            265                            270

Asp Leu Asp Leu Arg Glu Ile Thr Val Lys Gly Ser Phe Trp Gly Thr  
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Ser Met Asp Leu Arg Glu Ala Phe Glu Leu Ala Ala Gln Gly Lys Val  
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Lys Pro Asn Val Ala His Ala Pro Leu Ser Glu Leu Pro Lys Tyr Met  
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Glu Lys Leu Arg Ala Gly Gly Tyr Glu Gly Arg Val Val Phe Asn Pro  
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&lt;210&gt; 25

&lt;211&gt; 2481

&lt;212&gt; DNA

<213> *Candida albicans*

&lt;400&gt; 25

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 aatcgtgaag atgaagaaa tagcttgaat gaagtgggtt acgacgatat tggagggtgt 660  
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<211> 826

<212> PRT

<213> Candida albicans

<400> 26

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 35 40 45

Val Ile Thr Met Ser Ser Asn Thr Met Glu Leu Leu Gln Leu Phe Arg  
 50 55 60

Gly Asp Thr Val Leu Val Lys Gly Lys Lys Arg Lys Asp Thr Val Leu  
 65 70 75 80

Ile Val Leu Ala Asp Asp Asp Met Pro Asp Gly Val Ala Arg Val Asn  
 85 90 95

Arg Cys Val Arg Asn Asn Leu Arg Val Arg Leu Gly Asp Ile Val Thr  
 100 105 110

Val His Pro Cys Pro Asp Ile Lys Tyr Ala Asn Arg Ile Ser Val Leu  
 115 120 125

Pro Ile Ala Asp Thr Val Glu Gly Ile Asn Gly Ser Leu Phe Asp Leu  
 130 135 140

Tyr Leu Lys Pro Tyr Phe Val Glu Ala Tyr Arg Pro Val Arg Lys Gly  
 145 150 155 160

Asp Leu Phe Thr Val Arg Gly Gly Met Arg Gln Val Glu Phe Lys Val  
 165 170 175

Val Glu Val Asp Pro Glu Glu Ile Ala Ile Val Ala Gln Asp Thr Ile  
 180 185 190

Ile His Cys Glu Gly Glu Pro Ile Asn Arg Glu Asp Glu Glu Asn Ser  
 195 200 205  
 Leu Asn Glu Val Gly Tyr Asp Asp Ile Gly Gly Cys Lys Lys Gln Met  
 210 215 220  
 Ala Gln Ile Arg Glu Leu Val Glu Leu Pro Leu Arg His Pro Gln Leu  
 225 230 235 240  
 Phe Lys Ser Ile Gly Ile Lys Pro Pro Lys Gly Ile Leu Met Tyr Gly  
 245 250 255  
 Pro Pro Gly Thr Gly Lys Thr Ile Met Ala Arg Ala Val Ala Asn Glu  
 260 265 270  
 Thr Gly Ala Phe Phe Phe Leu Ile Asn Gly Pro Glu Ile Met Ser Lys  
 275 280 285  
 Met Ala Gly Glu Ser Glu Ser Asn Leu Arg Lys Ala Phe Glu Glu Ala  
 290 295 300  
 Glu Lys Asn Ser Pro Ser Ile Ile Phe Ile Asp Glu Ile Asp Ser Ile  
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 Ala Pro Lys Arg Asp Lys Thr Asn Gly Glu Val Glu Arg Arg Val Val  
 325 330 335  
 Ser Gln Leu Leu Thr Leu Met Asp Gly Met Lys Ala Arg Ser Asn Val  
 340 345 350  
 Val Val Ile Ala Ala Thr Asn Arg Pro Asn Ser Ile Asp Pro Ala Leu  
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 Arg Arg Phe Gly Arg Phe Asp Arg Glu Val Asp Ile Gly Val Pro Asp  
 370 375 380  
 Ala Glu Gly Arg Leu Glu Ile Leu Arg Ile His Thr Lys Asn Met Lys  
 385 390 395 400  
 Leu Ala Asp Asp Val Asp Leu Glu Ala Ile Ala Ser Glu Thr His Gly  
 405 410 415  
 Phe Val Gly Ala Asp Ile Ala Ser Leu Cys Ser Glu Ala Ala Met Gln  
 420 425 430  
 Gln Ile Arg Glu Lys Met Asp Leu Ile Asp Leu Glu Glu Glu Thr Ile  
 435 440 445

Asp Thr Glu Val Leu Asn Ser Leu Gly Val Thr Gln Asp Asn Phe Arg  
 450 455 460  
 Phe Ala Leu Gly Asn Ser Asn Pro Ser Ala Leu Arg Glu Thr Val Val  
 465 470 475 480  
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 485 490 495  
 Lys Asn Glu Leu Lys Glu Thr Val Glu Tyr Pro Val Leu His Pro Asp  
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 Gln Tyr Gln Lys Phe Gly Leu Ala Pro Thr Lys Gly Val Leu Phe Phe  
 515 520 525  
 Gly Pro Pro Gly Thr Gly Lys Thr Leu Leu Ala Lys Ala Val Ala Thr  
 530 535 540  
 Glu Val Ser Ala Asn Phe Ile Ser Val Lys Gly Pro Glu Leu Leu Ser  
 545 550 555 560  
 Met Trp Tyr Gly Glu Ser Glu Ser Asn Ile Arg Asp Ile Phe Asp Lys  
 565 570 575  
 Ala Arg Ala Ala Ala Pro Thr Val Val Phe Leu Asp Glu Leu Asp Ser  
 580 585 590  
 Ile Ala Lys Ala Arg Gly Gly Ser His Gly Asp Ala Gly Gly Ala Ser  
 595 600 605  
 Asp Arg Val Val Asn Gln Leu Leu Thr Glu Met Asp Gly Met Asn Ala  
 610 615 620  
 Lys Lys Asn Val Phe Val Ile Gly Ala Thr Asn Arg Pro Asp Gln Ile  
 625 630 635 640  
 Asp Pro Ala Leu Leu Arg Pro Gly Arg Leu Asp Gln Leu Ile Tyr Val  
 645 650 655  
 Pro Leu Pro Asp Glu Pro Ala Arg Leu Ser Ile Leu Gln Ala Gln Leu  
 660 665 670  
 Arg Asn Thr Pro Leu Glu Pro Gly Leu Asp Leu Asn Glu Ile Ala Lys  
 675 680 685  
 Ile Thr His Gly Phe Ser Gly Ala Asp Leu Ser Tyr Ile Val Gln Arg  
 690 695 700

Ser Ala Lys Phe Ala Ile Lys Asp Ser Ile Glu Ala Gln Val Lys Ile  
 705 710 715 720  
 Asn Lys Ile Lys Glu Glu Lys Glu Lys Val Lys Thr Glu Asp Val Asp  
 725 730 735  
 Met Lys Val Asp Glu Val Glu Glu Glu Asp Pro Val Pro Tyr Ile Thr  
 740 745 750  
 Arg Ala His Phe Glu Glu Ala Met Lys Thr Ala Lys Arg Ser Val Ser  
 755 760 765  
 Asp Ala Glu Leu Arg Arg Tyr Glu Ser Tyr Ala Gln Gln Leu Gln Ala  
 770 775 780  
 Ser Arg Gly Gln Phe Ser Ser Phe Arg Phe Asn Glu Asn Ala Gly Ala  
 785 790 795 800  
 Thr Asp Asn Gly Ser Ala Ala Gly Ala Asn Ser Gly Ala Ala Phe Gly  
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 Asn Val Glu Glu Glu Asp Asp Leu Tyr Ser  
 820 825

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 <212> DNA  
 <213> Candida albicans

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&lt;210&gt; 28

&lt;211&gt; 466

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 28

Met Ser Ala Phe Arg Ser Ile Gln Arg Ser Thr Asn Val Ala Lys Ser  
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 Thr Phe Lys Asn Ser Ile Arg Thr Tyr Ala Ser Ala Glu Pro Thr Leu  
 20 25 30  
 Lys Gln Arg Leu Glu Glu Ile Leu Pro Ala Lys Ala Glu Glu Val Lys  
 35 40 45  
 Gln Phe Lys Lys Glu His Gly Lys Thr Val Ile Gly Glu Val Leu Leu  
 50 55 60  
 Glu Gln Ala Tyr Gly Gly Met Arg Gly Ile Lys Gly Leu Val Trp Glu  
 65 70 75 80  
 Gly Ser Val Leu Asp Pro Ile Glu Gly Ile Arg Phe Arg Gly Arg Thr  
 85 90 95  
 Ile Pro Asp Ile Gln Lys Glu Leu Pro Lys Ala Pro Gly Gly Glu Glu  
 100 105 110  
 Pro Leu Pro Glu Ala Leu Phe Trp Leu Leu Leu Thr Gly Glu Val Pro  
 115 120 125  
 Thr Asp Ala Gln Thr Lys Ala Leu Ser Glu Glu Phe Ala Ala Arg Ser  
 130 135 140

Ala Leu Pro Lys His Val Glu Glu Leu Ile Asp Arg Ser Pro Ser His  
 145 150 155 160  
 Leu His Pro Met Ala Gln Phe Ser Ile Ala Val Thr Ala Leu Glu Ser  
 165 170 175  
 Glu Ser Gln Phe Ala Gln Ala Tyr Ala Lys Gly Ala Asn Lys Ser Glu  
 180 185 190  
 Tyr Trp Lys Tyr Thr Tyr Glu Asp Ser Ile Asp Leu Leu Ala Lys Leu  
 195 200 205  
 Pro Thr Ile Ala Ala Lys Ile Tyr Arg Asn Val Phe His Asp Gly Lys  
 210 215 220  
 Leu Pro Ala Ala Ile Asp Ser Lys Leu Asp Tyr Gly Ala Asn Leu Ala  
 225 230 235 240  
 Ser Leu Leu Gly Phe Gly Asp Asn Lys Glu Phe Val Glu Leu Met Arg  
 245 250 255  
 Leu Tyr Leu Thr Ile His Ser Asp His Glu Gly Gly Asn Val Ser Ala  
 260 265 270  
 His Thr Thr His Leu Val Gly Ser Ala Leu Ser Ser Pro Phe Leu Ser  
 275 280 285  
 Leu Ala Ala Gly Leu Asn Gly Leu Ala Gly Pro Leu His Gly Arg Ala  
 290 295 300  
 Asn Gln Glu Val Leu Glu Trp Leu Phe Lys Leu Arg Glu Glu Leu Asn  
 305 310 315 320  
 Gly Asp Tyr Ser Lys Glu Ala Ile Glu Lys Tyr Leu Trp Glu Thr Leu  
 325 330 335  
 Asn Ser Gly Arg Val Val Pro Gly Tyr Gly His Ala Val Leu Arg Lys  
 340 345 350  
 Thr Asp Pro Arg Tyr Thr Ala Gln Arg Glu Phe Ala Leu Lys His Met  
 355 360 365  
 Pro Asp Tyr Glu Leu Phe Lys Leu Val Ser Asn Ile Tyr Glu Val Ala  
 370 375 380  
 Pro Gly Val Leu Thr Lys His Gly Lys Thr Lys Asn Pro Trp Pro Asn  
 385 390 395 400

Val Asp Ser His Ser Gly Val Leu Leu Gln Tyr Tyr Gly Leu Thr Glu  
 405 410 415

Gln Ser Phe Tyr Thr Val Leu Phe Gly Val Ser Arg Ala Phe Gly Val  
 420 425 430

Leu Pro Gln Leu Ile Leu Asp Arg Gly Ile Gly Met Pro Ile Glu Arg  
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Pro Lys Ser Phe Ser Thr Glu Lys Tyr Ile Glu Leu Val Lys Asn Ile  
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Asn Lys  
 465

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 <211> 2862  
 <212> DNA  
 <213> Candida albicans

<400> 29

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 aaccctacca atgatgttaa gttttcacaa atatttttgg atttgaagaa acgctcacag 180  
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ttacaagata ttttgcatca tgttgaaagc aaatgggttg gtgggtttat ttcaggtatt 1680  
ttcactaatg acaatgacgt tgaaaatgaa tccaagaacg tgtttcataa attcaaacia 1740  
gatttaatga aaattttgaa agattgttta accgtaagt acgataaatc gaatatagag 1800  
aggtttcttc agtttaatga atttatttat tactgctttt actcaatgga ggaatataat 1860  
tatgaattgg ttgatgattt gataaaattt ataactataa atatgaattc tcatggcaga 1920  
atagttaatt ttggcactaa tgttaaaatt aataaattac acgaattaat taagaatttg 1980  
attgataaag ttaataaaaa caaacaatat gtgactagca acaacaaaaa caacagcaac 2040  
aacaacagca acaacaacag caacagcaac aattcccaac atattgtttt gatacctaatt 2100  
gccaaactgtt ccaattttcc atgggaatcg atgggaattt ttcgtagtaa atcaatttca 2160  
agaatgccat caattcatat gttacttgat ctagtcaaatt caaacaccaa taacaagaac 2220  
aagttaattg ttgttgataa atctaatttg tattatttga ttaatcccag tgggtgattta 2280  
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ttattgttag gttgttcac agttaaaatta gataattgta attataacta taattccagt 2580  
atgttacaac cactgggtaa tttttataat tgggtgaact gtaaatcgtc aatgatactc 2640  
gggaatctat gggatgttac tgataaggat attgatattt ttacactttc attactacaa 2700  
aaatgggggt taatagatga ttataatggt agtggccatg attatggtat gaagaaattg 2760  
gatttgacta attgtgttgt tcaaagtcga agtaaatgta ctttgaaata cttgaatgga 2820  
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&lt;210&gt; 30

&lt;211&gt; 953

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 30

Met Ile Asp Glu Leu Ile Asp Ile Ile Glu Ile Leu Leu Ala Lys Ser  
1 5 10 15

Ile Lys Asp Glu Gln Phe Glu Asn Phe Leu Lys Phe Glu Tyr Cys Arg  
20 25 30

Ala Leu Leu Ser Gln Thr Asn Asn Asn Pro Thr Asn Asp Val Lys Phe  
35 40 45

Ser Gln Ile Phe Leu Asp Leu Lys Lys Arg Ser Gln Asn Trp Lys Ser  
50 55 60

Phe Asp Asp Ile Ile Gln Leu Ser Leu Leu Gln Leu Gln Tyr Cys Ile  
65 70 75 80

Tyr Ala Lys Asn Ser Ile Lys Ala Lys Asp Arg Phe Asn Gly Ile Leu  
85 90 95



Gln Thr Leu Leu Lys Lys Pro Gln Phe Asn Ile Ser Lys Ser Lys Asn  
 100 105 110

Leu Pro Ile Val Ser Lys Leu Gln Asn Phe Leu Ile Leu Gly Lys Phe  
 115 120 125

Gln Leu Leu Ala Cys His Val Asn Asn His Ile Ile His Asn Lys Ile  
 130 135 140

Glu Ala Phe Asn Asn Ile Lys Thr Gly Ile Gln Leu Leu Tyr Ser Ile  
 145 150 155 160

Val Lys Lys Leu Pro Thr Asn Ile Asn Lys Thr Leu Trp Gln Glu Leu  
 165 170 175

Asn Trp Glu Ile Thr Arg Leu Leu Phe Asp Ser Tyr Lys Leu Ala Ile  
 180 185 190

Asp Leu Ser Ile Asp Ile Gly Ile Ser Arg Asp Ile Pro Leu Phe Leu  
 195 200 205

Asn Glu Trp Val Lys Leu Asn Asn Ser Ile Asp Asn Asp Val Pro Ile  
 210 215 220

Val Asn Cys Ile Asn Glu Phe Glu Ile Gly Arg Tyr Gly Leu Leu Ser  
 225 230 235 240

Asn Asn Glu Phe Gln Lys Tyr Ile Arg Ile Ala Gln Gly Arg Leu Gly  
 245 250 255

Tyr Ser Leu Val Lys Asn Asn Ser Ala Val Gln Gln Tyr Ile Asn Arg  
 260 265 270

Asp Arg Asp Asp Glu Ile Cys Gly His Ala Ser Ser Ser Arg Gln Leu  
 275 280 285

Lys Ser Leu Val Arg Thr Ile Phe Asn Ser Asp Asn Ser Leu Ser Glu  
 290 295 300

Leu Ser Lys Ser Val Gln Leu Leu Pro Cys Ile Ile Gly Asp Ser Ser  
 305 310 315 320

Thr Met Cys Ser Lys Glu Leu Leu Asp Lys Leu Val Gln Leu Lys Asn  
 325 330 335

Glu Ile Leu Thr Glu Val Thr Asn Tyr Glu Lys Ser Ser Ser Leu Ser  
 340 345 350

Leu Asn Gln Gln Gln Gln Leu Ile Asn Asn Leu Asn Gln Val Val Cys  
 355 360 365  
 Leu Leu Ser Ser Leu Thr Ser Phe Lys Gly Asp Gly Leu Leu Ser Glu  
 370 375 380  
 Val Tyr Tyr Leu Gln Asp Tyr Val Arg Asn Leu Pro Phe Ala Asn Glu  
 385 390 395 400  
 Arg Lys Leu Met Asp Ser Ser Lys Gln Asp Glu Ser Asn Asn Leu Leu  
 405 410 415  
 Pro Arg Ala Leu Asp Phe Asn Gln Val Val Glu Asp Pro Ser Asn Thr  
 420 425 430  
 Thr Ile Asn Asn Ser Met Ile Asp Phe Asn Val Asp Leu Gln Leu Tyr  
 435 440 445  
 Leu Pro His Asn Trp Ile Leu Val Thr Leu Asp Ile Cys Gln Asn Thr  
 450 455 460  
 Gly Asp Leu Leu Ile Ser Lys Leu Thr Lys Gly Ser Pro Asn Pro Ile  
 465 470 475 480  
 Phe Met Arg Leu Pro Leu Ser Arg Phe Pro Ser Ser Leu Gly Phe Gln  
 485 490 495  
 Gln Leu Met Gln Asn Phe Glu Lys Ile Ile Asp Asp Ser Asn Leu Ser  
 500 505 510  
 Thr Lys Arg Lys Thr Thr Ser Lys Ile Leu Thr Val Glu Asp Arg Lys  
 515 520 525  
 Gln Trp Trp Arg Ser Arg Phe Thr Leu Asp Phe Gln Leu Gln Asp Ile  
 530 535 540  
 Leu His His Val Glu Ser Lys Trp Phe Gly Gly Phe Ile Ser Gly Ile  
 545 550 555 560  
 Phe Thr Asn Asp Asn Asp Val Glu Asn Glu Ser Lys Asn Val Phe His  
 565 570 575  
 Lys Phe Lys Gln Asp Leu Met Lys Ile Leu Lys Asp Cys Leu Thr Val  
 580 585 590  
 Ser Asp Asp Lys Ser Asn Ile Glu Arg Phe Leu Gln Phe Asn Glu Phe  
 595 600 605

Ile Tyr Tyr Cys Phe Tyr Ser Met Glu Glu Tyr Asn Tyr Glu Leu Val  
 610 615 620

Asp Asp Leu Ile Lys Phe Ile Thr Ile Asn Met Asn Ser His Gly Arg  
 625 630 635 640

Ile Val Asn Phe Gly Thr Asn Val Lys Ile Asn Lys Leu His Glu Leu  
 645 650 655

Ile Lys Asn Leu Ile Asp Lys Val Asn Lys Asn Lys Gln Asn Val Thr  
 660 665 670

Ser Asn Asn Lys Asn Asn Ser Asn Asn Asn Ser Asn Asn Asn Ser Asn  
 675 680 685

Ser Asn Asn Ser Gln His Ile Val Leu Ile Pro Asn Ala Asn Cys Ser  
 690 695 700

Asn Phe Pro Trp Glu Ser Met Glu Phe Leu Arg Ser Lys Ser Ile Ser  
 705 710 715 720

Arg Met Pro Ser Ile His Met Leu Leu Asp Leu Val Lys Ser Asn Thr  
 725 730 735

Asn Asn Lys Asn Lys Leu Met Phe Val Asp Lys Ser Asn Leu Tyr Tyr  
 740 745 750

Leu Ile Asn Pro Ser Gly Asp Leu Ile Arg Ser Glu Asn Arg Phe Lys  
 755 760 765

Lys Leu Phe Glu Ser Asn His Leu Trp Arg Gly Glu Ile Gly Lys Leu  
 770 775 780

Ser Ser Asn Glu His Glu Asp Tyr Gln Asp Ser Ile Leu Cys Glu Ile  
 785 790 795 800

Leu Lys Ser His Leu Phe Val Tyr Ile Gly His Gly Gly Cys Asp Gln  
 805 810 815

Tyr Ile Lys Val Ser Lys Leu Phe Lys Lys Cys Gly Asn Asn Gln Asp  
 820 825 830

Leu Ser Asn Lys Leu Pro Pro Ser Leu Leu Leu Gly Cys Ser Ser Val  
 835 840 845

Lys Leu Asp Asn Cys Asn Tyr Asn Tyr Asn Ser Ser Met Leu Gln Pro  
 850 855 860

Ser Gly Asn Ile Tyr Asn Trp Leu Asn Cys Lys Ser Ser Met Ile Leu  
 865 870 875 880

Gly Asn Leu Trp Asp Val Thr Asp Lys Asp Ile Asp Ile Phe Thr Leu  
 885 890 895

Ser Leu Leu Gln Lys Trp Gly Leu Ile Asp Asp Tyr Asn Gly Ser Gly  
 900 905 910

His Asp Tyr Gly Met Lys Lys Leu Asp Leu Thr Asn Cys Val Val Gln  
 915 920 925

Ser Arg Ser Lys Cys Thr Leu Lys Tyr Leu Asn Gly Ser Ala Pro Val  
 930 935 940

Val Tyr Gly Leu Pro Met Tyr Leu Lys  
 945 950

<210> 31

<211> 1443

<212> DNA

<213> Candida albicans

<400> 31

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 ctataatcga tctattcaca gtatttgatg ccattttgat ggtgatgaat gatgtgatgt 120  
 gatgctcatc ttattgggag ttcaaaaaaa aaaagttaca ctcgaaaaaa aaaaaatagc 180  
 attataaata gaagctttac tatcttatag aacaaaacaa aaaacactat cttctaatta 240  
 ataatggatg attttgatag agatttagat aatgagttgg aatttagtca taaatcaacg 300  
 aaaggaaata aggttcacg cacttttgaa agtatgaatt tgaaacctga tcttttgaaa 360  
 ggaatatatg cctatggatt tgaagcacca tctgctatc aatctagggc tattatgcag 420  
 atcatcagtg gtagagacac aatagcacag gcacaatctg gaactggtaa aactgctact 480  
 ttttctattg gtatgcttga gggttatagat actaaatcaa aagagtgtca agcacttatt 540  
 ttgtctccta ctagagagtt ggcaattcaa atacaaaatg tggatcatgca tttaggagat 600  
 tatatgaaca ttcacaccca tgcctgtatt ggtgggaaaa atgtcgggtga ggatgttaag 660  
 aaattgcagc aagggcaaca aatagttagt gggacaccag gtagagtgat tgatgtgata 720  
 aaaagaagaa atctacaaac tagaaatatt aaggttctta ttttagatga agctgatgaa 780  
 ctttttacaa aagggtttaa agaacagatc tacgaaatct acaaacattt accaccttcg 840  
 gttcaagtag tagttgttag tgccactttg ccacgtgaag tattggagat gacaagtaag 900  
 tttaccactg atccagtga aatcttggtg aagagggatg agatttcgct tctgggaatc 960  
 aaacaatatt atgttcaatg tgaacgtgaa gattggaagt ttgatacact atgtgatttg 1020  
 tatgacaacc ttacaataac tcaagcagtg atattttgta ataccaaatt gaaggtgaat 1080  
 tggcttgctg atcaaatgaa aaagcaaac tttactgttg tggcaatgca tggatgatag 1140  
 aaacaagatg aacgagattc aattatgaac gatttttagaa gggggaattc aagagtatta 1200  
 atatctacag atgtttgggc aagaggtatt gatgtccaac aagtctcgtt ggtaataaat 1260  
 tatgatttgc ccaccgataa ggaaaactat attcatagaa ttggacgacg aggtagattt 1320  
 ggtagaaagg gaacagctat aaacttgata actaaagatg atgtgggtcac tttaaaagaa 1380

ttggagaaat attattcaac gaaaattaag gaaatgccaa tgaatattaa tgatataatg 1440  
taa 1443

<210> 32

<211> 399

<212> PRT

<213> Candida albicans

<400> 32

Met Asp Asp Phe Asp Arg Asp Leu Asp Asn Glu Leu Glu Phe Ser His  
1 5 10 15

Lys Ser Thr Lys Gly Ile Lys Val His Arg Thr Phe Glu Ser Met Asn  
20 25 30

Leu Lys Pro Asp Leu Leu Lys Gly Ile Tyr Ala Tyr Gly Phe Glu Ala  
35 40 45

Pro Ser Ala Ile Gln Ser Arg Ala Ile Met Gln Ile Ile Ser Gly Arg  
50 55 60

Asp Thr Ile Ala Gln Ala Gln Ser Gly Thr Gly Lys Thr Ala Thr Phe  
65 70 75 80

Ser Ile Gly Met Leu Glu Val Ile Asp Thr Lys Ser Lys Glu Cys Gln  
85 90 95

Ala Leu Ile Leu Ser Pro Thr Arg Glu Leu Ala Ile Gln Ile Gln Asn  
100 105 110

Val Val Met His Leu Gly Asp Tyr Met Asn Ile His Thr His Ala Cys  
115 120 125

Ile Gly Gly Lys Asn Val Gly Glu Asp Val Lys Lys Leu Gln Gln Gly  
130 135 140

Gln Gln Ile Val Ser Gly Thr Pro Gly Arg Val Ile Asp Val Ile Lys  
145 150 155 160

Arg Arg Asn Leu Gln Thr Arg Asn Ile Lys Val Leu Ile Leu Asp Glu  
165 170 175

Ala Asp Glu Leu Phe Thr Lys Gly Phe Lys Glu Gln Ile Tyr Glu Ile  
180 185 190

Tyr Lys His Leu Pro Pro Ser Val Gln Val Val Val Val Ser Ala Thr  
195 200 205

Leu Pro Arg Glu Val Leu Glu Met Thr Ser Lys Phe Thr Thr Asp Pro  
 210 215 220  
 Val Lys Ile Leu Val Lys Arg Asp Glu Ile Ser Leu Ser Gly Ile Lys  
 225 230 235 240  
 Gln Tyr Tyr Val Gln Cys Glu Arg Glu Asp Trp Lys Phe Asp Thr Leu  
 245 250 255  
 Cys Asp Leu Tyr Asp Asn Leu Thr Ile Thr Gln Ala Val Ile Phe Cys  
 260 265 270  
 Asn Thr Lys Leu Lys Val Asn Trp Leu Ala Asp Gln Met Lys Lys Gln  
 275 280 285  
 Asn Phe Thr Val Val Ala Met His Gly Asp Met Lys Gln Asp Glu Arg  
 290 295 300  
 Asp Ser Ile Met Asn Asp Phe Arg Arg Gly Asn Ser Arg Val Leu Ile  
 305 310 315 320  
 Ser Thr Asp Val Trp Ala Arg Gly Ile Asp Val Gln Gln Val Ser Leu  
 325 330 335  
 Val Ile Asn Tyr Asp Leu Pro Thr Asp Lys Glu Asn Tyr Ile His Arg  
 340 345 350  
 Ile Gly Arg Ser Gly Arg Phe Gly Arg Lys Gly Thr Ala Ile Asn Leu  
 355 360 365  
 Ile Thr Lys Asp Asp Val Val Thr Leu Lys Glu Leu Glu Lys Tyr Tyr  
 370 375 380  
 Ser Thr Lys Ile Lys Glu Met Pro Met Asn Ile Asn Asp Ile Met  
 385 390 395

&lt;210&gt; 33

&lt;211&gt; 825

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 33

aacccacct tcaaagacaa agaagatttc gtcaagcaaa cgaatgtcag agcagaaaag 60  
 aaccaagaac taatcaaatt tgcccgtag aaccttaacc atttaccatt caccgaaaaa 120  
 gacggagggtg catgggaaaa ctatgaacga atgatcagtg gtatgtctta caactgttta 180  
 caaaaagaat tggaacaac acgtatgtct tgcagagact acatgttgga ctacggcagt 240  
 ttcagaacta gagattataa aacaacccaa gaatttcttg atgcaaaata caaacattta 300

gaaagtttca ttggacatgt tggcaaaaat gcatttatgg aatatccaat ctattttgat 360  
 tatgggttta acacttattt ggggtataat ttctattcca attacaattt gacaattttg 420  
 gatgtttcca tagtcagaat tggtaataat gtcaagtgtg gtcccaatgt atctatcctt 480  
 accccaacac acccagtgga tcccactttg cgctatgac aattggaaaa tgccttgcct 540  
 gtgacggtgg gtaacggggt ctggttgtgt ggaagctgta ccattcttgg tggggtgaca 600  
 gtaggtgatg gcagcattgt ggctgctggg gcagttgtca acaaggacgt tccaccaaac 660  
 actgtagttg cgggagttcc tgctagggtg gtttaagcagc tagaacctag agaccctaac 720  
 tttgacacta tggcagtttt gaaacaatat ggtatgggtt atatagatta gtaattagat 780  
 ttgatgtaat gtacacgact acactatttg ctgggtgtctg ttttt 825

<210> 34

<211> 206

<212> PRT

<213> Candida albicans

<400> 34

Met Ile Ser Gly Met Leu Tyr Asn Cys Leu Gln Lys Glu Leu Glu Thr  
 1 5 10 15

Thr Arg Met Ser Cys Arg Asp Tyr Met Leu Asp Tyr Gly Ser Phe Arg  
 20 25 30

Thr Arg Asp Tyr Lys Thr Thr Gln Glu Phe Leu Asp Ala Lys Tyr Lys  
 35 40 45

His Leu Glu Ser Phe Ile Gly His Val Gly Lys Asn Ala Phe Met Glu  
 50 55 60

Tyr Pro Ile Tyr Phe Asp Tyr Gly Phe Asn Thr Tyr Leu Gly Asp Asn  
 65 70 75 80

Phe Tyr Ser Asn Tyr Asn Leu Thr Ile Leu Asp Val Ser Ile Val Arg  
 85 90 95

Ile Gly Asn Asn Val Lys Cys Gly Pro Asn Val Ser Ile Leu Thr Pro  
 100 105 110

Thr His Pro Val Asp Pro Thr Leu Arg Tyr Asp Gln Leu Glu Asn Ala  
 115 120 125

Leu Pro Val Thr Val Gly Asn Gly Val Trp Leu Cys Gly Ser Cys Thr  
 130 135 140

Ile Leu Gly Gly Val Thr Val Gly Asp Gly Ser Ile Val Ala Ala Gly  
 145 150 155 160

Ala Val Val Asn Lys Asp Val Pro Pro Asn Thr Val Val Ala Gly Val  
 165 170 175

Pro Ala Arg Val Val Lys Gln Leu Glu Pro Arg Asp Pro Asn Phe Asp  
180 185 190

Thr Met Ala Val Leu Lys Gln Tyr Gly Met Gly Tyr Ile Asp  
195 200 205



20

25

30

Gln Ile Ser Ile Ala Lys Val Asp Glu Asp Gly Arg Ala Ile Ala Gly  
 35 40 45

Glu Asn Ile Thr Tyr Ala Leu Ser Gly Tyr Val Arg Gly Arg Gly Glu  
 50 55 60

Ala Asp Asp Ser Leu Asn Arg Leu Ala Gln Gln Asp Gly Leu Leu Lys  
 65 70 75 80

Asn Val Trp Ser Tyr Ser Arg  
 85

&lt;210&gt; 39

&lt;211&gt; 1685

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 39

ctgtttatta aatggatata tgtaaacca tgaacttcgg tttatcagaa aaattggtgc 60  
 tggtagctat ggtttgattt accttggtga aaatatctac actaaacaac aatttgctgc 120  
 taaaatgggt cttgaacagc cattactcaa acaaagcaa caacaacaac aaagtcac 180  
 tggacataaa ggagaatcta gtatgaacaa acaataata ctgcaagaat tttatcaata 240  
 ttttttaaac aatagtatgc cacaaccag aaatttggtgac ttgaattacc ttcgagacaa 300  
 cggacatgat tgcccccttt tgactgaaat ctcattacat ttaaaagtac atcaacaccc 360  
 aaacatagcg actattcatc aagtattaaa cattgaagat tttgccataa taatattgat 420  
 ggatcatttt gagcaaggag atttgttcac taatattcatt gatagacaaa tattcaccaa 480  
 taatagtcac agaaaagttc caagaacaga ttttgaaacc caattattaa tgaagaatgc 540  
 catgttacaa ttgatagaag ccattgaata ttgtcacgaa aataatattt accattgtga 600  
 tttaaaacca gaaaacatta tggtagata taatccatac tatgttcgtc caactatcaa 660  
 taacaataat aacaatggag aagatgattt atgctatgcc aacagtatta ttgactataa 720  
 tgaattacac ctggtgttga ttgattttgg ttttagctatg gactctgcta ccatttggtg 780  
 taattcatgt cgtggatcgt cattttacat ggcaccagaa agaaccacca attataacac 840  
 scatcgttta atcaaccaat taattgatat gaatcaatat gagtcaattg aaatcaatgg 900  
 gacaacagtg acaaaatcaa actgtaaata tttacctaca ttgggtgggg atatttggtc 960  
 attgggagta ttgttcatta atatcacttg ttcaagaac ccatggccca ttgcatcatt 1020  
 tgataataat caaaataatg aagtgtttta gaattatatg ttgaataata acaaggctgt 1080  
 tttgagcaaa atcttaccba tttctcaca atttaatcgc ttattagata gaattttcaa 1140  
 attgaatcct aatgatagaa tagatttacc aactttatac aaagaagtta ttcgttgtga 1200  
 tttcttcaaa gatgatcatt actactatgc ccaacatcaa catcatcaca atcacaatca 1260  
 aatcaataat gcttacaatc actatcagaa acaacctaata caagcaagac ctactgcaaa 1320  
 ccaacaattg tataaccac cggaaccac cacttataat tcatacgcta gtgatatgga 1380  
 agaagatgaa attagtgtg atgagtttta ttctgatgaa gaagatgaag atattgaaga 1440  
 ctatgaagag gaagaggaag agtattttgg taatgagcaa caacaacaac agcaagtcac 1500  
 aacagtgaat ggtaattttg gtcaagttaa aggtacctgt tattacgata ccaaaacca 1560  
 aacaactaca tatataaaac caccagctgc atatacttta gagacgcta gtcaaagtgt 1620

tgaatactgt taagttgtac acataaataa ttaatgacaa ttaataataa cgattaataa 1680  
tatag 1685

<210> 40

<211> 537

<212> PRT

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Ser Asp Glu Glu Asp Glu Asp Ile Glu Asp Tyr Glu Glu Glu Glu Glu  
 465 470 475 480

Glu Tyr Phe Gly Asn Glu Gln Gln Gln Gln Gln Val Thr Thr Val  
 485 490 495

Asn Gly Asn Phe Gly Gln Val Lys Gly Thr Cys Tyr Tyr Asp Thr Lys  
 500 505 510

Thr Lys Thr Thr Thr Tyr Ile Lys Pro Pro Ala Ala Tyr Thr Leu Glu  
 515 520 525

Thr Pro Ser Gln Ser Val Glu Tyr Cys  
 530 535

<210> 41  
 <211> 848  
 <212> DNA  
 <213> Candida albicans

<400> 41  
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 gtaccaaaca acaaatcact tcaatcatcg acaacttgaa caaggctgat ttaccaaagg 120  
 atgtcgaagt tgtcatttgt ccacccgccc tttaccttgg tttagctgta gagcaaaaca 180  
 aacaaccaac tgttgccatt ggtgctcaaa atgtttttga caagtcatgt ggtgctttca 240  
 ctggtgaaac ctgtgcttct caaatcttgg atgttggtgc cagctggact ttaactgggc 300  
 acagtgaag aagaaccatt atcaaagaat ccgatgaatt cattgctgaa aaaaccaagt 360  
 ttgccttgga cactgggtgc aaagttattt tatgtattgg tgaaacctta gaggaaagaa 420  
 aaggtgggtg cactttggat gtttgtgcca gacaattgga tgctgtttcc aagattgttt 480  
 ctgattgggc aaacattggt gttgcttacg aacctgtttg ggcaattggg actgggtttag 540  
 ccgctacccc agaagatgct gaagaaaccc acaaagggtat tagagctcat ttggccaaga 600  
 ccattgggtg cgaacaagct gaaaaaacca gaatcttgta cgggtggttca gttaacggta 660  
 agaacgctaa ggatttcaaa gacaaagcaa atgttgatgg tttcttagtc ggtgggtgctt 720  
 cattaaaacc agaatttggt gatatcatca aatctagatt ataaacagta tattaaaaac 780  
 tatatgccta tagaatttag catgttggtg tgaatttgta atgaatctat aaaaatgtgc 840  
 tcatgaac 848

<210> 42  
 <211> 248  
 <212> PRT  
 <213> Candida albicans

<400> 42  
 Met Ala Arg Gln Phe Phe Val Gly Gly Asn Phe Lys Ala Asn Gly Thr  
 1 5 10 15

Lys Gln Gln Ile Thr Ser Ile Ile Asp Asn Leu Asn Lys Ala Asp Leu

20 25 30  
 Pro Lys Asp Val Glu Val Val Ile Cys Pro Pro Ala Leu Tyr Leu Gly  
 35 40 45  
 Leu Ala Val Glu Gln Asn Lys Gln Pro Thr Val Ala Ile Gly Ala Gln  
 50 55 60  
 Asn Val Phe Asp Lys Ser Cys Gly Ala Phe Thr Gly Glu Thr Cys Ala  
 65 70 75 80  
 Ser Gln Ile Leu Asp Val Gly Ala Ser Trp Thr Leu Thr Gly His Ser  
 85 90 95  
 Glu Arg Arg Thr Ile Ile Lys Glu Ser Asp Glu Phe Ile Ala Glu Lys  
 100 105 110  
 Thr Lys Phe Ala Leu Asp Thr Gly Val Lys Val Ile Leu Cys Ile Gly  
 115 120 125  
 Glu Thr Leu Glu Glu Arg Lys Gly Gly Val Thr Leu Asp Val Cys Ala  
 130 135 140  
 Arg Gln Leu Asp Ala Val Ser Lys Ile Val Ser Asp Trp Ser Asn Ile  
 145 150 155 160  
 Val Val Ala Tyr Glu Pro Val Trp Ala Ile Gly Thr Gly Leu Ala Ala  
 165 170 175  
 Thr Pro Glu Asp Ala Glu Glu Thr His Lys Gly Ile Arg Ala His Leu  
 180 185 190  
 Ala Lys Thr Ile Gly Ala Glu Gln Ala Glu Lys Thr Arg Ile Leu Tyr  
 195 200 205  
 Gly Gly Ser Val Asn Gly Lys Asn Ala Lys Asp Phe Lys Asp Lys Ala  
 210 215 220  
 Asn Val Asp Gly Phe Leu Val Gly Gly Ala Ser Leu Lys Pro Glu Phe  
 225 230 235 240  
 Val Asp Ile Ile Lys Ser Arg Leu  
 245

&lt;210&gt; 43

&lt;211&gt; 550

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 43

Met Ser Leu Asp Asn Ser Thr Glu Asn Arg Asp Leu Glu Glu Lys Glu  
1 5 10 15

Glu Ile Pro Lys Asn Glu His Asn Glu Gln Gly Glu Gln Asn Glu Asn  
20 25 30

Asn Glu His Ile Pro Thr Leu Glu Asp Lys Pro Leu Lys Glu Tyr Ile  
35 40 45

Gly Ile Ser Ile Leu Cys Phe Leu Ile Ala Phe Gly Gly Phe Val Phe  
50 55 60

Gly Phe Asp Thr Gly Thr Ile Ser Gly Phe Ile Asn Met Thr Asp Phe  
65 70 75 80

Leu Glu Arg Phe Gly Gly Thr Lys Ala Asp Gly Thr Leu Tyr Phe Ser  
85 90 95

Asn Val Arg Thr Gly Leu Leu Ile Gly Leu Phe Asn Val Gly Cys Ala  
100 105 110

Ile Gly Ala Leu Phe Leu Ser Lys Val Gly Asp Met Tyr Gly Arg Arg  
115 120 125

Val Gly Ile Met Thr Ala Met Ile Ile Tyr Ile Val Gly Ile Ile Val  
130 135 140

Gln Ile Ala Ser Gln His Ala Trp Tyr Gln Ile Met Ile Gly Arg Ile  
145 150 155 160

Ile Thr Gly Leu Ala Val Gly Met Leu Ser Val Leu Cys Pro Leu Phe  
165 170 175

Ile Ser Glu Val Ser Pro Lys His Leu Arg Gly Thr Leu Val Tyr Cys  
180 185 190

Phe Gln Leu Met Ile Thr Leu Gly Ile Phe Leu Gly Tyr Cys Thr Ser  
195 200 205

Tyr Gly Thr Lys Lys Tyr Ser Asp Ser Arg Gln Trp Arg Ile Pro Leu  
210 215 220

Gly Leu Cys Phe Ala Trp Ala Leu Cys Leu Leu Gly Gly Met Val Arg  
225 230 235 240

Met Pro Glu Ser Pro Arg Tyr Leu Val Gly Lys Asp Arg Ile Asp Asp  
 245 250 255

Ala Lys Ile Ser Leu Ala Lys Thr Asn Lys Val Ser Pro Glu Asp Pro  
 260 265 270

Ala Leu Tyr Arg Glu Leu Gln Leu Ile Gln Ala Gly Val Glu Arg Glu  
 275 280 285

Arg Leu Ala Gly Lys Ala Ser Trp Gly Ala Leu Ile Thr Gly Lys Pro  
 290 295 300

Arg Ile Leu Glu Arg Val Ile Val Gly Gly Met Leu Gln Ser Leu Gln  
 305 310 315 320

Gln Leu Thr Gly Asp Asn Tyr Phe Phe Tyr Tyr Ser Thr Thr Ile Phe  
 325 330 335

Lys Ser Val Gly Leu Asn Asp Ser Phe Glu Thr Ser Ile Ile Leu Gly  
 340 345 350

Val Ile Asn Phe Ala Ser Thr Phe Val Gly Ile Tyr Ala Ile Glu Arg  
 355 360 365

Leu Gly Arg Arg Leu Cys Leu Leu Thr Gly Ser Val Ala Met Ser Ile  
 370 375 380

Cys Phe Leu Ile Tyr Ser Leu Ile Gly Thr Gln His Leu Tyr Ile Asp  
 385 390 395 400

Gln Pro Gly Gly Pro Thr Arg Lys Pro Asp Gly Asn Ala Met Ile Phe  
 405 410 415

Ile Thr Ala Leu Tyr Val Phe Phe Phe Ala Ser Thr Trp Ala Gly Gly  
 420 425 430

Val Tyr Ser Ile Val Ser Glu Leu Tyr Pro Leu Lys Val Arg Ser Lys  
 435 440 445

Ala Met Gly Phe Ala Asn Ala Cys Asn Trp Leu Trp Gly Phe Leu Ile  
 450 455 460

Ser Phe Phe Thr Ser Phe Ile Thr Asp Ala Ile His Phe Tyr Tyr Gly  
 465 470 475 480

Phe Val Phe Met Gly Cys Leu Val Phe Ser Ile Phe Phe Val Tyr Phe  
 485 490 495

Met Ile Tyr Glu Thr Lys Gly Leu Thr Leu Glu Glu Ile Asp Glu Leu  
 500 505 510

Tyr Ser Thr Lys Val Val Pro Trp Lys Ser Ala Gly Trp Val Pro Pro  
 515 520 525

Ser Asp Glu Glu Met Val Arg Ala Lys Gly Tyr Thr Gly Asp Ile His  
 530 535 540

Ala Asp Glu Glu Gln Val  
 545 550

<210> 44

<211> 508

<212> DNA

<213> Candida albicans

<400> 44

ttcatgatta tatgatttca tttaatatat tgatttaata tatatatatta attactcata 60  
 tagtcgtatt acacctgtag cccaattcat aagggtcatg cggattagtc ttcagcctct 120  
 acttcccata atatatctat tatgcatcac taattatagt aggcccgacc ataggtcggg 180  
 cttacttaaa tagtcgaggg ttgcgttcat tatataacta aataaaatac cacttggcat 240  
 gaactgacga caacaatgta acgcctgtat atactcgttc aggtaatgag tatatatattca 300  
 agaattggta aggtgttagg ggtatcatcc aattaaacag cataatccac tgtacctgta 360  
 tataaccgtc taatgtattg catttcatcc gtgaggacgt actagtctgg cgggtgtactt 420  
 caagtattaa cgtaccata atgaaagtta taggtttata aaccataac tatcttacat 480  
 atacgtagta cacatagttt acggctac 508

<210> 45

<211> 863

<212> DNA

<213> Candida albicans

<400> 45

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 cgataaagaa agaaagaatc aggtaccacg aggagtgttt ttgagaaaaa caactcgtaa 120  
 attaatgaat ctagtcttc tatacttgaa taatttttga gttttctgga aaagacacct 180  
 gttccagttt caaattaaac aagaatgtga aaagaataaa atttgattta ttctagcctg 240  
 ttaataatcc aggaaaactc aattttcgta attggcaact tgtccgagtg gttaaggaga 300  
 aagattagaa atcttttggg ctttgccgc gcagggtcga gtcctgcagt tgtcgttatt 360  
 ttttttgggt tactctctat tttaaaattt aaaactaate aactgaaact ggagtacctg 420  
 ccatgatatg agtaaatact tttttgatat taaaaatcta tataaaactc cctatttatt 480  
 ttttaattta aaccagata ttgtcccaat aatagttttt tgtttgaact tattgctttg 540  
 tatgaacctt gttagttaa tctttccaat ttcatactct cttagtggc cacatcagtg 600  
 gtcattgaa taattctgat cttgaagtgt accagatgta ttctgacaaa actgcacacg 660  
 gaccagtc aatgcattat agatatcttg atttaaagtt caccgaatat atcgaaatc 720  
 tttattggcc atctcatctc atcttcttgc aataaattct taaacgctac tttttctcaa 780

accttattat cccctctagat actcttccaa atcttcaggt tcaaatatca ctttaacctat 840  
caatgaacaa ctagggcaaa cag 863

<210> 46

<211> 925

<212> DNA

<213> Candida albicans

<400> 46

atgggtgcta cttgcccttt acggaaagtg gctacacacc gcaatggggt accgatttgg 60  
gaagctagta gggctaccag agctacaaa gtattgtggg agagttgggt acagtacaca 120  
ttgttacgca atgagttacc aattcgggaa gctagtaggg ctaccagagc taggttccag 180  
ttaccaattc gggaagctag tagagctacc agagctgggt tccagttacc gatttaggaa 240  
gtgtgttgca agcagggcta ccaaatatgg gtggcaacac atatggtaat aagtgtacc 300  
aatgtgggtg caaaaaattt tgccaagtaa tttgtatggc aataacagaa gtgttggcgg 360  
attcgaactc aggaatcttt ggtgtgtaaa aaaaaagcaa tagcgactac gctacaagag 420  
gcaatcgatt attattataa agtgggaagt atatatatgt tgctgggggg gggtaggggc 480  
gctgcgcgcc cctgactttg acggggccga cgcggtttg ggttgtgatg gggcggtaaa 540  
taataaggat tctccctccc tttttctctt tccccccct cctcctccc ctttccctt 600  
ttccccgagt ctacaaatct acaagaggcc cgacggtgga ggcctgaggc cgaagggtcga 660  
aggccgacaa agatgggtgg gtgggtggga ggttgtgttc ggggcgtagc cccgagaaaa 720  
ttttggaata cagggccagg agggtagggg aaatggggaa aatgggggat ttgggaggga 780  
atggggaagg aagaagaaga aaaaagtggg ggaaaggaga agattttttt tgggagaaaa 840  
aatttttttt ataccaccga gaagtgtgag aggatacgat ggggtgcgaca ggggtagag 900  
ctgttgacaa cgttatatgg gggag 925

<210> 47

<211> 78

<212> PRT

<213> Candida albicans

<400> 47

Met Gly Ala Thr Cys Pro Leu Arg Lys Val Ala Thr His Arg Asn Gly  
1 5 10 15

Leu Pro Ile Trp Glu Ala Ser Arg Ala Thr Arg Ala Thr Lys Val Leu  
20 25 30

Trp Glu Ser Trp Val Gln Tyr Thr Leu Leu Arg Asn Glu Leu Pro Ile  
35 40 45

Arg Glu Ala Ser Arg Ala Thr Arg Ala Arg Phe Gln Leu Pro Ile Arg  
50 55 60

Glu Ala Ser Arg Ala Thr Arg Ala Gly Phe Gln Leu Pro Ile  
65 70 75



<210> 48  
 <211> 81  
 <212> PRT  
 <213> Candida albicans

<400> 48  
 Met Gly Tyr Arg Phe Gly Lys Leu Val Gly Leu Pro Glu Leu Pro Lys  
           1                  5                  10                  15  
 Tyr Cys Gly Arg Val Gly Tyr Ser Thr His Cys Tyr Ala Met Ser Tyr  
                   20                  25                  30  
 Gln Phe Gly Lys Leu Val Gly Leu Pro Glu Leu Gly Ser Ser Tyr Gln  
           35                  40                  45  
 Phe Gly Lys Leu Val Glu Leu Pro Glu Ser Gly Ser Ser Tyr Arg Phe  
           50                  55                  60  
 Arg Lys Cys Val Ala Ser Arg Ala Thr Lys Tyr Gly Trp Gln His Ile  
           65                  70                  75                  80

Trp

<210> 49  
 <211> 759  
 <212> DNA  
 <213> Candida albicans

<400> 49  
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 gattattgcc atgccctgag gatgagttta gttttttaat ttttgaaaaa tgtccaaaac 120  
 tgggttgct gtataggagg ggtaagaatt tgccattctg cccctttggg tgggtcagtc 180  
 aaaaaagag gtatcactct ggttcaaacg ggaaacaaca gaaaatggga taaaaataat 240  
 ctccagacca aacttagtag taacagccat tttagttgta ctggtatacc ctacacaagt 300  
 tgtccatttt gtatggggaa gggaatttta gacaaaattt tttttttgaa tttcgctaag 360  
 tgtcaagacc cgcaaaagtc accttttttc gttttcaact atggcagagg ctcacctttt 420  
 gtctggtgca cagccaaatt gatattgttg gtgcgcactg gaaaaacagt ttgttagtgg 480  
 acacgttttt gcagtgtgaa actgcgctcg gaggtactat atgcgaaagc agaaaagaca 540  
 attgcaagaa tacagagagt tcttctctgg gctattgcaa tgtgtttaag gccaaagtcga 600  
 cgagtgggga gagtctggaa gtgatataca catcacgacc tactttatac gctacgttcg 660  
 gcatgggcga gccactgtac ggtggcaagc ctgaacagtc ccacaccaga tatctaacga 720  
 ttctgtgtat gggcactgat ggatttagtg gattactag 759

<210> 50  
 <211> 902  
 <212> DNA

<213> *Candida albicans*

<400> 50

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atgtcctgtg aagacgaaca tcacaaccac aatcatgggc ataaccaaaa tcacaatcat 60
gttgctccta ttctacaac agctggacaa tcattaaata ataaaattga tacatctaaa 120
gtgacagctc tcaacatggc caactctgct gacgatctag caaaagtttt caaagattcg 180
actaaaaaat atcaaatcaa accaattatc aaatcagaca gtgatgaaca aatgattatc 240
aacattccat ttcttaatgg tagtgtcaaa ttgtattcga taattctacg taccaatggg 300
gatttgtatt gtccaaaaac aataaaatta ttcaaaaatg acacatcaat tgattttgat 360
aatgtggatt cgaagaaacc aatacagggtg ttaactcadc ctcaagttgg tgttgcta 420
aatgatagcg atgatcttcc agagtttttg gaatcaaata acgatgacga ttttgctgaa 480
cattatgtgt ctgcacataa attcactggg gtaaatcaat tgacaatatt tattgaagat 540
atztatgatg aaggagaaga agagtgtcat ttacattcaa ttgaattgag aggggaattc 600
actgaattaa acaaagaccc tgcattaca ttatatgaac tggctgctaa tctgctgat 660
cataagaatt taacgattgt tgaaaatcaa aatctagcat aaaacaaaga agtgaaagg 720
atcagataag ctggttacat tacaattgat ctaatttaga atctcaagg attttaaatt 780
gccgttttgc gataatataa catggtcaag aacgttgaat cgattacgtt aatggtttag 840
ctaattgatt tttaggatcg agtatttaga gtgaataaac aataaacaag aatgatgaat 900
tg

```

902

<210> 51

<211> 233

<212> PRT

<213> *Candida albicans*

<400> 51

```

Met Ser Cys Glu Asp Glu His His Asn His Asn His Gly His Asn Gln
  1                      5                      10                      15

```

```

Asn His Asn His Val Ala Pro Ile Pro Thr Thr Ala Gly Gln Ser Leu
          20                      25                      30

```

```

Asn Asn Lys Ile Asp Thr Ser Lys Val Thr Ala Leu Asn Met Ala Asn
          35                      40                      45

```

```

Ser Ala Asp Asp Leu Ala Lys Val Phe Lys Asp Ser Thr Lys Lys Tyr
          50                      55                      60

```

```

Gln Ile Lys Pro Ile Ile Lys Ser Asp Ser Asp Glu Gln Met Ile Ile
          65                      70                      75                      80

```

```

Asn Ile Pro Phe Leu Asn Gly Ser Val Lys Leu Tyr Ser Ile Ile Leu
          85                      90                      95

```

```

Arg Thr Asn Gly Asp Leu Tyr Cys Pro Lys Thr Ile Lys Leu Phe Lys
          100                     105                     110

```

```

Asn Asp Thr Ser Ile Asp Phe Asp Asn Val Asp Ser Lys Lys Pro Ile

```

115                      120                      125  
 Gln Val Leu Thr His Pro Gln Val Gly Val Ala Asn Asn Asp Ser Asp  
 130                      135                      140  
 Asp Leu Pro Glu Phe Leu Glu Ser Asn Asn Asp Asp Asp Phe Val Glu  
 145                      150                      155                      160  
 His Tyr Val Ser Arg His Lys Phe Thr Gly Val Asn Gln Leu Thr Ile  
 165                      170                      175  
 Phe Ile Glu Asp Ile Tyr Asp Glu Gly Glu Glu Glu Cys His Leu His  
 180                      185                      190  
 Ser Ile Glu Leu Arg Gly Glu Phe Thr Glu Leu Asn Lys Asp Pro Val  
 195                      200                      205  
 Ile Thr Leu Tyr Glu Ser Ala Ala Asn Pro Ala Asp His Lys Asn Leu  
 210                      215                      220  
 Thr Ile Val Glu Asn Gln Asn Leu Ala  
 225                      230

&lt;210&gt; 52

&lt;211&gt; 1833

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 52

atggcatcgt ctaataatgg atttgagtca ataaatctag cttccactat tctgggacct 60  
 tatcaagaag aagacacccc tatcaaactg ttacattcta tccccgcttc cacctccgaa 120  
 gatgaagatg aactcgatcc cgaagagttc attttaaata aagtagataa accagctaca 180  
 aaagactcac atgtgctgta caataaattt ctggataagc atataagtga tgagcaacta 240  
 tcacacttac tgcacaatca taaacccaat ctagtgaact ccacaacttt aattgattct 300  
 atcaaagaaa gtgaactggt atataatacc atggacagtt tgatgataaa atccatcaat 360  
 tttcctgcag ccatgtacca gtcaaagac aacaattcac aatcaccaat cgagtattta 420  
 tctaacagag taaaattgct cacacaagag ttatacgaag attcagtcaa atatggcaag 480  
 tttctacaga gtggtataaa tcatatatat caattacgaa gtaggatttt acagaccttt 540  
 gatcagttgt cagagagtca ctattcttta aatgaactat ataataaaga catgtcttac 600  
 gcagaaacat tacacggatc tttcaagaaa tgggatcaac aaagaaataa agtattgtcc 660  
 aaagtgaat ctataaaaag tgatacaagc aaacatggag ccaaattatt caccttatta 720  
 gatgaagtta atgatgttga tgacgagatc aaacttttgg aagcaaaact acagcagctt 780  
 cgatctaaaa aagaaatttt aaataaagaa attgaagata ccagcagtggt tttggaaaagc 840  
 agaacagcaa aatatgttga catatttaag gatttggaaa acaaaggtag gtcagcaatt 900  
 actgatttcc ttcagtccaa tgggtgtccc gaaaaagaaa ttgatacaat tgtgagattc 960  
 tcacctgttg atattacgat ttctagcaac tattcactga aaaaggaacc aaagaaagag 1020  
 attcacatta caaaagagtc aattcctcaa aatgagtcgg ctagtaaaacc cgcaaatact 1080

```

ccagtatag gtatgcaacc gtttataata cctgaagcag aagccaatac caaaacaccg 1140
gatttgcaat caatgaacca cgatcatggg cctactcctt ttgaaaaagg atatgctatg 1200
gggacacaaa attctacggc gttgaaaaac aaaatgaatc atataatgaa aaagttttta 1260
gattctttac caataactcc accatcaaat atctcaacaa tgccagccac ttcacgtatt 1320
aaagtggatg atttatcaaa tacaatctct aaaagattag atttggatcc aataatgggt 1380
tttttggaac acaaagttgc tgcattacat gatttggcca taaaatcatc tcaaatgct 1440
gcattattcc atgaatttgg gagaatatgg gagagcgta caaaactaat gaattctcag 1500
gaagaaaagt tggagagtat tctcaacgat gattcgaatt ctaaattagt tacacgtatc 1560
ttgaattcca ctttagaaca attgaaatcc accctatctg cattgaagag caaccctgta 1620
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atagaacagg ctgtgaaact tgtatcgctt gaccttcgaa ctataggaga actcaattct 1740
agcgggggcc taccctcttc gtcttcaaaa cctacaagtc aagtgtaccc agttagtacc 1800
agtgcacca agctgactac aaaaatggaa taa 1833

```

&lt;210&gt; 53

&lt;211&gt; 610

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 53

```

Met Ala Ser Ser Asn Asn Gly Phe Glu Ser Ile Asn Leu Ala Ser Thr
  1             5             10             15

```

```

Ile Ser Gly Pro Tyr Gln Glu Glu Asp Thr Pro Ile Lys Arg Leu His
          20             25             30

```

```

Ser Ile Pro Ala Ser Thr Ser Glu Asp Glu Asp Glu Leu Asp Pro Glu
          35             40             45

```

```

Glu Phe Ile Leu Asn Lys Val Asp Lys Pro Ala Thr Lys Asp Ser His
          50             55             60

```

```

Val Ser Tyr Asn Lys Phe Ser Asp Lys His Ile Ser Asp Glu Gln Leu
          65             70             75             80

```

```

Ser His Leu Leu Asp Asn His Lys Pro Asn Leu Val Thr Thr Thr Thr
          85             90             95

```

```

Leu Ile Asp Ser Ile Lys Glu Ser Glu Ser Leu Tyr Asn Thr Met Asp
          100             105             110

```

```

Ser Leu Met Ile Lys Ser Ile Asn Phe Pro Ala Ala Met Tyr Gln Ser
          115             120             125

```

```

Asn Asp Asn Asn Ser Gln Ser Pro Ile Glu Tyr Leu Ser Asn Arg Val
          130             135             140

```

```

Lys Leu Leu Thr Gln Glu Leu Tyr Glu Asp Ser Val Lys Tyr Gly Lys

```

145                      150                      155                      160  
 Phe Leu Gln Ser Gly Asn Asn His Ile Tyr Gln Leu Arg Ser Arg Ile  
                          165                      170                      175  
 Leu Gln Thr Phe Asp Gln Leu Ser Glu Ser His Tyr Ser Leu Asn Glu  
                          180                      185                      190  
 Leu Tyr Asn Lys Asp Met Ser Tyr Ala Glu Thr Leu His Gly Ser Phe  
                          195                      200                      205  
 Lys Lys Trp Asp Gln Gln Arg Asn Lys Val Leu Ser Lys Val Lys Ser  
                          210                      215                      220  
 Ile Lys Ser Asp Thr Ser Lys His Gly Ala Lys Leu Phe Thr Leu Leu  
 225                      230                      235                      240  
 Asp Glu Val Asn Asp Val Asp Asp Glu Ile Lys Leu Leu Glu Ala Lys  
                          245                      250                      255  
 Leu Gln Gln Leu Arg Ser Lys Lys Glu Ile Leu Asn Lys Glu Ile Glu  
                          260                      265                      270  
 Asp Thr Ser Ser Val Leu Glu Ser Arg Thr Ala Lys Tyr Val Asp Ile  
                          275                      280                      285  
 Phe Lys Asp Leu Glu Asn Lys Gly Arg Ser Ala Ile Thr Asp Phe Leu  
                          290                      295                      300  
 Gln Ser Asn Gly Val Pro Glu Lys Glu Ile Asp Thr Ile Val Arg Phe  
 305                      310                      315                      320  
 Ser Pro Val Asp Ile Thr Ile Ser Ser Asn Tyr Ser Ser Lys Lys Glu  
                          325                      330                      335  
 Pro Lys Lys Glu Ile His Ile Thr Lys Glu Ser Ile Pro Gln Asn Glu  
                          340                      345                      350  
 Ser Ala Ser Lys Pro Ala Asn Thr Pro Ser Ile Gly Met Gln Pro Phe  
                          355                      360                      365  
 Ile Ile Pro Glu Ala Glu Ala Asn Thr Lys Thr Pro Asp Leu Gln Ser  
                          370                      375                      380  
 Met Asn His Asp His Gly Pro Thr Pro Phe Glu Lys Gly Tyr Ala Met  
 385                      390                      395                      400  
 Gly Thr Gln Asn Ser Thr Ala Leu Lys Asn Lys Met Asn His Ile Met

```
<210> 54
<211> 75
<212> PRT
<213> Candida albicans
<400> 54
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Met Ser Thr Tyr Phe Ala Val Ser Leu Ser Lys Thr Ser Ser Val Ser  
 1 5 10 15

Ser Ile Ser Leu Phe Lys Ile Ser Phe Leu Asp Arg Ser Cys Cys Ser  
 20 25 30

Phe Ala Ser Lys Ser Leu Ile Ser Ser Ser Thr Ser Leu Thr Ser Ser  
 35 40 45

Asn Lys Val Asn Asn Leu Ala Pro Cys Leu Leu Val Ser Leu Phe Ile  
 50 55 60

Asp Phe Thr Leu Asp Asn Thr Leu Phe Leu Cys  
 65 70 75

<210> 55

<211> 1164

<212> DNA

<213> Candida albicans

<400> 55

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 aacataaaac taccacttcg gtcattcacg ataaagaaac ggtacctgga attccagcaa 120  
 ttggtgctgg acttgagtcg taatctaggc attgatagtc gagattttcc atatgaatta 180  
 cctgggaaac ggatcaactg gcttaacaag accagtattg ttgaggagag aaaagtggga 240  
 cttgcagaat ttctcaataa cctcattcaa gactcaacac ttcagaatga acgagaagtg 300  
 ttgtcgtttt tgcaattgcc gtctaatttt agattcacca aggatatgtt acagaataat 360  
 cgagcagact tggattctgt gcaaaataac tggtagcatg tatatcgtaa gttgaaactg 420  
 gatatactca acgaatcgtc tagcagcatt agtgaacaga tacatattcg tgatcgcatt 480  
 agtcgggtct accaaccacg gattctcgac ttggtcaggg ctattggtac agataaagaa 540  
 gagggcctaa agaagaagca gttggtttcc caattacaag agagtataga taatttggtta 600  
 gtacaggaag tccccgatc aaagagggtg ttgggtggag cagttaagga aacgccagag 660  
 acattaccat taaacaataa agaacttctt caacaccaag taaaattca tcaaaaccaa 720  
 gacaaagaac tagaccagct taggggtgta attgcccggc agaaacagat tggcgagcta 780  
 attaatgcag aagtagagga acagaatgaa atgttggata ggtttaatga agaggtcgac 840  
 tacacgtcca gcaaaatcaa gcaagcaaga cgcagagcta agaagatatt atagtaattt 900  
 gttcgctact tcgatattat ctgccattga cgttattctt gcaggttggc ccaattgttc 960  
 gtttgaaagt ttttcgaggt cttcagcgtc taatgcccta tctgagctct cgccatcgag 1020  
 tttccaaaac ccgccgatat tttgaaagaa tctttgaatg ccaaaccgtc gtggcgggaa 1080  
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<210> 56

<211> 297

<212> PRT

<213> Candida albicans

&lt;400&gt; 56

Met Ser Thr Ile Thr Ile Pro His Asp Ile Glu Ile Gly Gly Ser Thr  
 1 5 10 15

Tyr Tyr Gln Ile Asn Ile Lys Leu Pro Leu Arg Ser Phe Thr Ile Lys  
 20 25 30

Lys Arg Tyr Ser Glu Phe Gln Gln Leu Val Ser Asp Leu Ser Arg Asn  
 35 40 45

Leu Gly Ile Asp Ser Arg Asp Phe Pro Tyr Glu Leu Pro Gly Lys Arg  
 50 55 60

Ile Asn Trp Leu Asn Lys Thr Ser Ile Val Glu Glu Arg Lys Val Gly  
 65 70 75 80

Leu Ala Glu Phe Leu Asn Asn Leu Ile Gln Asp Ser Thr Leu Gln Asn  
 85 90 95

Glu Arg Glu Val Leu Ser Phe Leu Gln Leu Pro Ser Asn Phe Arg Phe  
 100 105 110

Thr Lys Asp Met Leu Gln Asn Asn Arg Ala Asp Leu Asp Ser Val Gln  
 115 120 125

Asn Asn Trp Tyr Asp Val Tyr Arg Lys Leu Lys Ser Asp Ile Leu Asn  
 130 135 140

Glu Ser Ser Ser Ser Ile Ser Glu Gln Ile His Ile Arg Asp Arg Ile  
 145 150 155 160

Ser Arg Val Tyr Gln Pro Arg Ile Leu Asp Leu Val Arg Ala Ile Gly  
 165 170 175

Thr Asp Lys Glu Glu Ala Leu Lys Lys Lys Gln Leu Val Ser Gln Leu  
 180 185 190

Gln Glu Ser Ile Asp Asn Leu Leu Val Gln Glu Val Pro Arg Ser Lys  
 195 200 205

Arg Val Leu Gly Gly Ala Val Lys Glu Thr Pro Glu Thr Leu Pro Leu  
 210 215 220

Asn Asn Lys Glu Leu Leu Gln His Gln Val Gln Ile His Gln Asn Gln  
 225 230 235 240

Asp Lys Glu Leu Asp Gln Leu Arg Val Leu Ile Ala Arg Gln Lys Gln  
 245 250 255



Ile Gly Glu Leu Ile Asn Ala Glu Val Glu Glu Gln Asn Glu Met Leu  
 260 265 270

Asp Arg Phe Asn Glu Glu Val Asp Tyr Thr Ser Ser Lys Ile Lys Gln  
 275 280 285

Ala Arg Arg Arg Ala Lys Lys Ile Leu  
 290 295

<210> 57

<211> 7707

<212> DNA

<213> Candida albicans

<400> 57

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 atcactataa acaatgggat actgttcaat ggaatatcat ttcacacaaa acgatatcta 180  
 atatcggtag ggtcattgag atttagacta tggggtaata gtaaaatgac catcattgat 240  
 gacttaacta tcaagttatt gccaaatgtg aaaaataacc aaaaacaaaa tactcaagaa 300  
 aagcgcaatg actatagttt caaagatcct actgctccag tggccaatat attcccccaa 360  
 aatagaattg gcaaatatgt ggtctccagg cttattcgac acctcccgaa aatgaatttg 420  
 gaactaagac aaaccgctat tatcactccg tctgagaaca agactataat agagtattta 480  
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 1890 1895 1900  
 Lys Asp Asp Leu Ser Ser Thr Ser Glu Ile Ile Arg Arg Phe Thr Ser  
 1905 1910 1915 1920  
 Glu Gly Val Lys Ser Gln Thr Ser Thr Ser Lys Asp Ile Thr Ser Gln  
 1925 1930 1935  
 Gln Lys Leu Asp Asn Phe Asn Thr Ile Leu Arg Glu Thr Arg Pro Asp  
 1940 1945 1950  
 Glu Lys Val Val Glu Asp Tyr Leu Ile Asp Val Ile Ala Pro Gln Ile  
 1955 1960 1965  
 Gln Leu Gln Ser Glu Asp Tyr Pro Asp Ser Val Val Leu Ile Ser Thr  
 1970 1975 1980  
 Pro Ser Ile Lys Gly Lys Ile Leu Ser Ile Met Asp Ser Arg Asn Asn  
 1985 1990 1995 2000

Ala Asn Gln Ile Leu Leu Glu Thr Arg Tyr Gly Ile Leu Leu Lys Asp  
 2005 2010 2015

Ala Asn Val Phe Val Leu Asn Lys Glu Asp Ile Val Gly Cys Pro Asp  
 2020 2025 2030

Met Leu Ser Ile Ser Asn Pro Tyr Gly Ala Lys Ser Asn Trp Pro Pro  
 2035 2040 2045

Trp Leu Gly Thr Glu Ile Thr Gln Asn Gly Lys Trp Ala Gly Ala Asn  
 2050 2055 2060

Asn Leu Leu Ile Glu Lys Leu Ser Val Met Thr Met Cys Tyr Glu Ser  
 2065 2070 2075 2080

Glu Ile Leu Ser Ser Lys Leu Ser Pro Asn Ala Gln Asp Ser Asp Gln  
 2085 2090 2095

Glu Glu Gln Glu Asn Tyr Asn Asp Asp Asn Ser Lys Gln Ala Pro Leu  
 2100 2105 2110

Arg Leu Gly Ile Asp Met Pro Ser Val Val Ile Thr Ser Thr Ser Ser  
 2115 2120 2125

Gln Tyr Phe Thr Leu Tyr Val Ile Ile Val Ser Leu Leu Phe Tyr Ser  
 2130 2135 2140

Glu Pro Met Ser Lys Val Ile His Lys Lys Ile Glu Lys Met Lys Phe  
 2145 2150 2155 2160

Ser Ile Asp Phe Glu Asp Leu Gly Ala Leu Thr Ser Arg Leu Thr Lys  
 2165 2170 2175

Met Gln Gln His His Lys Leu Leu Lys Val Leu Ser Asn Asn Tyr Ser  
 2180 2185 2190

Phe Arg Gln Gly Lys Leu Asn Asn Glu Asp Leu Asn Asn Tyr Leu Gln  
 2195 2200 2205

Val Asn Leu Glu Arg Gly Glu Ile Ala Ser Asp Ile Tyr Leu Leu Leu  
 2210 2215 2220

Arg Thr Leu Leu Thr Gly Asp Phe Ala Ser Asp Thr Ser Asn Asn Leu  
 2225 2230 2235 2240

Ser Met Xaa Trp Leu Ile Arg Ala Asp Glu Ile Ile Leu Gln Ile Leu  
 2245 2250 2255

Glu Asp Asp Arg Thr Pro Ile Met Asp Leu Ala Leu Ala Gln Gly Met  
 2260 2265 2270  
 Tyr Thr Arg Lys Glu Leu Glu Ser Gly Ser Asn Ile Asn Lys Leu His  
 2275 2280 2285  
 Ile Gly Thr Met Arg Gly Phe Asn Leu Ile Glu Ser Ala Arg Tyr Pro  
 2290 2295 2300  
 Asp Phe Ile Lys Pro Ile Thr Glu Ser Ser Ser Gln Asn Leu Ile Glu  
 2305 2310 2315 2320  
 Leu Ala Trp Thr Met Asn Lys Ser Val Gly Gly Ile Lys Ile Ile Glu  
 2325 2330 2335  
 Asn Val Phe Val Asn Ala Ala Pro Leu Asn Ile Lys Leu Asp Glu Ile  
 2340 2345 2350  
 Thr Gly Asp Lys Leu Met Lys Phe Ile Thr Tyr Ser Asn Ser Gly Asn  
 2355 2360 2365  
 Leu Glu Asp Ser Lys Ile Ile Ala Val Ser Asn Glu Lys Asn Lys Asp  
 2370 2375 2380  
 Asn Ile Lys Asp Asn Ser Glu Asp Glu Asp Tyr Gly Leu Ile Thr Glu  
 2385 2390 2395 2400  
 Asn Glu Gly Ile Asn Lys Gly Pro Lys Phe Glu Glu Met Ser Gln Ser  
 2405 2410 2415  
 Ser Asn Met Lys Arg Ser Leu Thr Met Leu Ser Ser Lys Lys Ser Ser  
 2420 2425 2430  
 Ser Ser Ala Ser Ser Asn Asp Glu Ile Glu Asp Asn Glu Asp Val Glu  
 2435 2440 2445  
 Lys Met Ile Glu Arg Ser Lys Lys Tyr Phe Ser Val Val Ser Leu Asn  
 2450 2455 2460  
 Val Asn Ala Ile Thr Leu Glu Val Thr Leu Lys Leu Asn Lys Gly Phe  
 2465 2470 2475 2480  
 Lys Arg Ile Leu Asn Val Asn Asp Phe Arg Ile Asp Leu Pro Glu Phe  
 2485 2490 2495  
 Asn Ile Thr Asn Glu Ile Val Ser Tyr Met Asp Ile Ser Lys Met Leu  
 2500 2505 2510

Gln Ser Met Ile Thr Lys Met Ile Leu Gly His Val Gly Arg Leu Leu  
 2515 2520 2525

Gly Asn Lys Met Lys Ala Thr Lys Gly Lys Ser Lys Lys Ile Met Lys  
 2530 2535 2540

Lys Arg Lys Arg Ile Arg Ser Ile Ser Asp Val Arg Lys Glu Ile His  
 2545 2550 2555 2560

Val Ser Thr Glu Arg Gly Ala Asp  
 2565

<210> 59

<211> 2196

<212> DNA

<213> Candida albicans

<400> 59

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 ttaccggtca cagctaataa ttcatttgtc caagacttgt ttcaaagcag atttacccca 180  
 tatgtcaaat ttaaaattgt aacagacccc gcatcaaata ttttggagac tcatgtcatt 240  
 agacaagtgg cttttgtgga attggaatcg gccagtata tgtcaaagc tttaaaatgg 300  
 catgatttgt attataagac aaatagaaga gtaactgttg aagtggcaga ttttaatatg 360  
 tttcaaaatt gtattaaatt caatcaagaa catgaacgtg aaattatgca aatccaacaa 420  
 gaattcattg ctcagaaaca acaacaacgg caaccagac atatggctct tttagatgaa 480  
 tttgaaagaa accagcgcgg tcttggatca ccttgcac aaaaccatga tcaccacaat 540  
 cccaccaccac aacaacaaca acacatcat ttcaatccta atttaaacag accttcaggt 600  
 agatcaagtc ttccaataga tgaaacgtct cattcaagaa gactttcttt tgaagctcaa 660  
 ttacatcctc atcaacagac ccatggacag cgtattagac aaccatcttt tgacaatgca 720  
 ttcccagaca ctctcatcc accatttggg ggtgggtggg gtatgcgtca acaaattccat 780  
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 gttgatactt tatctaaaca acaagagatt gagaagaaac taatcaattt gaataaaact 960  
 acagttacaga ctttaggaga tgtagaacc cctgaagaag ttcaagcaac tattaataaa 1020  
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 ccaccaccac cacctcaaca acaacaacaa cagcaacctc cacaacaaca agatcagaac 1200  
 acaaagcaaa ctgcattaca tcaaccagat caactacaaa atcattcatc aaatatttct 1260  
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aatgatagtc gagcatcatc ttcttcttca aatagtagaa gatttgaatt tattcgagga 1800  
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 gatcagcaag atttgtcttc tactaacact gggtcagaag gtagaatgtg ggaaagagga 1980  
 agaggtagag gtagaggtgg tttcagtttc agaagcagag gtggtttcag aggtagagga 2040  
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 agatcaaaac caactcccgt tgaaaccaat gagtaa 2196

<210> 60

<211> 731

<212> PRT

<213> Candida albicans

<400> 60

Met Ala Ser Ile Ser Val Pro Ile Glu Lys Gly Ser Phe His Asp Gly  
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Asp Gly Phe Asn Gln His His Leu Gly Asp Pro Val Ile Ser Gly Pro  
 20 25 30

Pro Tyr Ile Ile Lys Leu Leu Asn Leu Pro Val Thr Ala Asn Asp Ser  
 35 40 45

Phe Val Gln Asp Leu Phe Gln Ser Arg Phe Thr Pro Tyr Val Lys Phe  
 50 55 60

Lys Ile Val Thr Asp Pro Ala Ser Asn Ile Leu Glu Thr His Val Ile  
 65 70 75 80

Arg Gln Val Ala Phe Val Glu Leu Glu Ser Ala Ser Asp Met Ser Lys  
 85 90 95

Ala Leu Lys Trp His Asp Leu Tyr Tyr Lys Thr Asn Arg Arg Val Thr  
 100 105 110

Val Glu Val Ala Asp Phe Asn Asp Phe Gln Asn Cys Ile Lys Phe Asn  
 115 120 125

Gln Glu His Glu Arg Glu Ile Met Gln Ile Gln Gln Glu Phe Ile Ala  
 130 135 140

Gln Lys Gln Gln Gln Arg Gln Pro Arg His Met Ala Leu Leu Asp Glu  
 145 150 155 160

Phe Glu Arg Asn Gln Arg Gly Pro Gly Ser Pro Leu His Gln Asn His  
 165 170 175

Asp His His Asn Pro His Pro Gln Gln Gln Gln His His His Phe Asn  
 180 185 190  
 Pro Asn Leu Asn Arg Pro Ser Gly Arg Ser Ser Leu Pro Ile Asp Glu  
 195 200 205  
 Thr Ser His Ser Arg Arg Leu Ser Phe Glu Ala Gln Leu His Pro His  
 210 215 220  
 Gln Gln Thr His Gly Gln Arg Ile Arg Gln Pro Ser Phe Asp Asn Ala  
 225 230 235 240  
 Phe Pro Asp Thr Pro His Pro Pro Phe Gly Gly Gly Gly Gly Met Arg  
 245 250 255  
 Gln Gln Ile His Pro Thr Asn Gln Pro Ala Val Pro Ser Ser Ala Pro  
 260 265 270  
 Ala Ser Lys Pro Phe Val Thr Pro Ile Ser Ser Ala Ser Thr Ser Ser  
 275 280 285  
 Arg Pro Ile Ser Asn Pro Phe Gly Ala Ala Lys Pro Val Asp Thr Leu  
 290 295 300  
 Ser Lys Gln Gln Glu Ile Glu Lys Lys Leu Ile Asn Leu Asn Lys Thr  
 305 310 315 320  
 Thr Val Gln Thr Leu Gly Asp Val Glu Thr Pro Glu Glu Val Gln Ala  
 325 330 335  
 Thr Ile Lys Lys Phe His Glu Asn Gly Ser Pro Lys Leu Arg Arg Ala  
 340 345 350  
 Ser Val Gly Thr Pro Arg Arg Leu Ser Ser Glu Lys Arg Pro Ser Val  
 355 360 365  
 Ser Ile Leu Arg Arg Asp Leu Pro Glu Arg Gln Gln Pro Pro Pro Pro  
 370 375 380  
 Pro Gln Gln Gln Gln Gln Gln Gln Pro Pro Gln Gln Gln Asp Gln Asn  
 385 390 395 400  
 Thr Lys Gln Thr Ala Leu His Gln Pro Asp Gln Leu Gln Asn His Ser  
 405 410 415  
 Ser Asn Ile Ser Ser Thr Gln Pro Ser Gly Glu Ser Pro Leu Ala Glu  
 420 425 430



Thr Gln Ser Leu Ser Thr Asn Pro Tyr Thr Ser Asn Gly Thr Gly Lys  
 435 440 445

Ser Leu Ala Gln Leu Leu Ser Glu Gln Ser Asp Ile Met Ser Ala Pro  
 450 455 460

Pro Ile Thr Gly Lys Lys Thr Pro Arg Ser Asn Ser Asn Thr Lys Lys  
 465 470 475 480

Pro Val Val Ala Ala Lys Pro Val Ile Leu Lys Lys Lys Thr Pro Thr  
 485 490 495

Ser Pro Pro Val Gln Arg Ile Asp Leu Thr Ile Lys Glu Ser Glu Tyr  
 500 505 510

Leu Lys Lys Gln Asp Glu Thr Asp Asp Leu Ile Asp Ala Asn Val Glu  
 515 520 525

Thr Lys Leu Glu Lys Leu Asp Leu Asn Ser Glu Thr Leu Ser Glu Asn  
 530 535 540

Gly Thr Lys Glu Ser Thr Lys Thr Arg Ile Asp Asn Pro Lys Arg Glu  
 545 550 555 560

Asn Asp Gln His Asp Asp Arg Pro Asn Phe Lys Asn Leu Asp Gln Leu  
 565 570 575

Val Gln Lys Arg Asn Asp Ser Arg Ala Ser Ser Ser Ser Ser Asn Ser  
 580 585 590

Arg Arg Phe Glu Phe Ile Arg Gly Leu Lys Glu Glu Asn Glu Arg Val  
 595 600 605

Pro Ser Pro Ser Ser Ser Ser Ser Ser Ser Ser Ala Thr Lys Thr Ser  
 610 615 620

Gln Asn Asn Phe Glu Lys Ser Ser Glu Ser Ala Ile Ser Arg Thr Asp  
 625 630 635 640

Asp Gln Gln Asp Leu Ser Ser Thr Asn Thr Gly Ser Glu Gly Arg Met  
 645 650 655

Trp Glu Arg Gly Arg Gly Arg Gly Arg Gly Phe Ser Phe Arg Ser  
 660 665 670

Arg Gly Gly Phe Arg Gly Arg Gly Ala Gly Phe Arg Gly Ser Gly Arg  
 675 680 685

Gly Gly Pro Arg Arg Arg Gly Gly Asn Gly Ala Ser Gly Ala Gly Gly  
 690 695 700

Thr Ala Ser Gly Ser Thr Gly Ser Ala Asn Tyr Asn Leu His Tyr Val  
 705 710 715 720

Arg Ser Lys Pro Thr Pro Val Glu Thr Asn Glu  
 725 730

<210> 61

<211> 1483

<212> DNA

<213> Candida albicans

<400> 61

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 cactgtatgt acctagatgg attaccaaga tctactacat aaaataataa aggagttcca 120  
 ctactcaaa gagttcaaac catgggatag cagtgttttg tatgagacgt tactacgac 180  
 agtattaact actttgatcg aacttttggg catagacaat ccacccagtt atctacacct 240  
 caccaccaac aatgatagta taggtgattt gaaaataaaa tactatggaa atgcattaag 300  
 caagtcaatc aacggtcata gcatgttgca atatcttgaa tcaaagcatg tatcgatatt 360  
 acaggccgtg gttgagatta ttaatacgcg atcatataga atcaaagagt cttattctgc 420  
 tgttttcaaa gacgtttctc atttatttga aaaactacta aaggaaagat atgaagctga 480  
 atctaatacta gaggattata tattgcagtg cttgatgtac gagacccaat tttaccaagg 540  
 aattgttgat aatgttttaa ctgccgatga caccgaaaaa ttggctagtt ttttggggac 600  
 acgactatct gaagaagatt cgatgttttag ctatagggat atagattatc cactagagtt 660  
 aaacattaat aatgaatctc ttgaaaagat atataaaatt ttcttaggag tcattggcac 720  
 caaaagattc gatatcaagg aggttgcgtc tgctgttggt ggtgtgtata aacgacacca 780  
 gagaatagat cattttgaaa agttggattc agatgagatt ttgggaaagt ttttcagaaa 840  
 tatattgccca caactgttcc agagtgtgac aaataagggt ttccgggaat ttcacaaaga 900  
 ggtagatgac ccaccatcgg acgtgctaga ccagctagat aatattgttg atgactttat 960  
 tgcggttgga attgaagggg tagatttggg ctttcgggct ttgttcagac actacataaa 1020  
 attcatgaac gaaatttttc cactgtggt cgaggatgct gaccgcgatt ttgttgcaag 1080  
 aattaatagt ttaattgctc aagtcttggg gtttaaagac gatgaaaaat cctgtgatat 1140  
 gaatcaagtg gtatctgaat ttgtttcatt acaaagtttg ctacttaaga ataactatct 1200  
 ttcaccatct acattattga tgcgtgcaag tactcacgat tactataaaa atttacagat 1260  
 cgtgaaaata acctttgatg gatggaatga gaattcaaag aggatattga aattggagaa 1320  
 cagcggcttt ttacaaagca agacattgcc aaagtattta aaattatggt actcaaaaag 1380  
 tatgaagttg aatgaattat gtaaccgggt agatgaattt tataatggag aactttgtcg 1440  
 gaaagtttgg cattgttgga gggcacaaca aagatgtcta taa 1483

<210> 62

<211> 468

<212> PRT

<213> Candida albicans

<400> 62

Met Asp Tyr Gln Asp Leu Leu His Lys Ile Il Lys Glu Phe His Ser  
 1 5 10 15  
 Leu Lys Glu Phe Lys Pro Trp Asp Ser Ser Val Leu Tyr Glu Thr Leu  
 20 25 30  
 Leu Arg Ser Val Leu Thr Thr Leu Ile Glu Leu Leu Gly Ile Asp Asn  
 35 40 45  
 Pro Pro Ser Tyr Leu His Leu Thr Thr Asn Asn Asp Ser Ile Gly Asp  
 50 55 60  
 Leu Lys Ile Lys Tyr Tyr Gly Asn Ala Leu Ser Lys Ser Ile Asn Gly  
 65 70 75 80  
 His Ser Met Leu Gln Tyr Leu Glu Ser Lys His Val Ser Ile Leu Gln  
 85 90 95  
 Ala Val Val Glu Ile Ile Asn Thr Arg Ser Tyr Arg Ile Lys Glu Ser  
 100 105 110  
 Tyr Ser Ala Val Phe Lys Asp Val Ser His Leu Phe Glu Lys Leu Leu  
 115 120 125  
 Lys Glu Arg Tyr Glu Ala Glu Ser Asn Leu Glu Asp Tyr Ile Leu Gln  
 130 135 140  
 Cys Leu Met Tyr Glu Thr Gln Phe Tyr Gln Gly Ile Val Asp Asn Val  
 145 150 155 160  
 Leu Thr Ala Asp Asp Thr Glu Lys Leu Ala Ser Phe Leu Gly Thr Arg  
 165 170 175  
 Leu Ser Glu Glu Asp Ser Met Phe Ser Tyr Arg Asp Ile Asp Tyr Pro  
 180 185 190  
 Leu Glu Leu Asn Ile Asn Asn Glu Ser Leu Glu Lys Ile Tyr Lys Ile  
 195 200 205  
 Phe Leu Gly Val Ile Gly Thr Lys Arg Phe Asp Ile Lys Glu Val Ala  
 210 215 220  
 Ser Ala Val Val Gly Val Tyr Lys Arg His Gln Arg Ile Asp His Phe  
 225 230 235 240  
 Glu Lys Leu Asp Ser Asp Glu Ile Leu Gly Lys Phe Phe Arg Asn Ile  
 245 250 255

Leu Pro Gln Ser Phe Gln Ser Val Thr Asn Lys Val Phe Arg Glu Phe  
 260 265 270  
 His Lys Glu Val Asp Asp Pro Pro Ser Asp Val Leu Asp Gln Leu Asp  
 275 280 285  
 Asn Ile Val Asp Asp Phe Ile Ala Val Gly Ile Glu Gly Val Asp Leu  
 290 295 300  
 Gly Phe Pro Ala Leu Phe Arg His Tyr Ile Lys Phe Met Asn Glu Ile  
 305 310 315 320  
 Phe Pro Thr Val Val Glu Asp Ala Asp Arg Asp Phe Val Ala Arg Ile  
 325 330 335  
 Asn Ser Leu Ile Ala Gln Val Leu Glu Phe Lys Asp Asp Glu Lys Ser  
 340 345 350  
 Cys Asp Ile Asn Gln Val Val Ser Glu Phe Val Ser Leu Gln Ser Leu  
 355 360 365  
 Leu Leu Lys Asn Asn Tyr Leu Ser Pro Ser Thr Leu Leu Met Arg Ala  
 370 375 380  
 Ser Thr His Asp Tyr Tyr Lys Asn Leu Gln Ile Val Lys Ile Thr Phe  
 385 390 395 400  
 Asp Gly Trp Asn Glu Asn Ser Lys Arg Ile Leu Lys Leu Glu Asn Ser  
 405 410 415  
 Gly Phe Leu Gln Ser Lys Thr Leu Pro Lys Tyr Leu Lys Leu Trp Tyr  
 420 425 430  
 Ser Lys Ser Met Lys Leu Asn Glu Leu Cys Asn Arg Val Asp Glu Phe  
 435 440 445  
 Tyr Asn Gly Glu Leu Cys Arg Lys Val Trp His Cys Trp Arg Ala Gln  
 450 455 460  
 Gln Arg Cys Leu  
 465

&lt;210&gt; 63

&lt;211&gt; 715

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 63

tgtttggttg taatagtatt tctatattac atttcacttt tgaagacaaa agaattttta 60  
 ggtacaaaat tgttgccaaa attttataaa aaattgtcaa atgaaaagaa gtatttccaa 120  
 atatattggt tttcatcaca acagttcata tcgccataga ccatttttaa tcttaagggt 180  
 gataccagtt aattggtgat ttctctgtta tagaccctgt cttaatctgt ctatttctgg 240  
 tategaatca aaatgtcgct cataatgtgc atgtcgcaaa gatgtcgtaa agttttgatt 300  
 tcatactcat cttaaatttt ttttagtgat tggcattttg ttctttcaca tagtttttat 360  
 ttctagttat caacctatca aatacacctc cacaacaatg catccaaata ataaaaattc 420  
 atttaaataca aaaaagaaat ttatagatcg tcgagaagcc aagtctcaag atataaaacg 480  
 tgcattaacc catagggcta gattaagaaa gaactatttc aaactattag aaaaagaagg 540  
 gttacaagag gagaggaagc ctgaagatga gaacgatata agaccaacca agaagaaggg 600  
 aataaatttt gaagaacgtg cagccattgt gaaacaacgt aaagaggaaa aacgtaaatt 660  
 caaactagca agtgtaacag caaaattgga aaagattgaa tctaattcga aagaa 715

&lt;210&gt; 64

&lt;211&gt; 106

&lt;212&gt; PRT

<213> *Candida albicans*

&lt;400&gt; 64

Met His Pro Asn Asn Lys Asn Ser Phe Lys Ser Lys Lys Lys Phe Ile  
 1 5 10 15  
 Asp Arg Arg Glu Ala Lys Ser Gln Asp Ile Lys Arg Ala Leu Thr His  
 20 25 30  
 Arg Ala Arg Leu Arg Lys Asn Tyr Phe Lys Leu Leu Glu Lys Glu Gly  
 35 40 45  
 Leu Gln Glu Glu Arg Lys Pro Glu Asp Glu Asn Asp Ile Arg Pro Thr  
 50 55 60  
 Lys Lys Lys Gly Ile Asn Phe Glu Glu Arg Ala Ala Ile Val Lys Gln  
 65 70 75 80  
 Arg Lys Glu Glu Lys Arg Lys Phe Lys Leu Ala Ser Val Gln Ala Lys  
 85 90 95  
 Leu Glu Lys Ile Glu Ser Asn Ser Lys Glu  
 100 105

&lt;210&gt; 65

&lt;211&gt; 147

&lt;212&gt; DNA

<213> *Candida albicans*

&lt;400&gt; 65

atgaagattt caccagagac agtaaataaa ctacaactgg atgcatcgtg tataagaaac 60  
 atctgtattt tagcacatgt cgaccacggt aaaacctcat tgagtgactc attattagcc 120  
 accaatggaa tcatttccca acgtatg 147

<210> 66

<211> 49

<212> PRT

<213> Candida albicans

<400> 66

Met Lys Ile Ser Pro Glu Thr Val Asn Lys Leu Gln Ser Asp Ala Ser  
 1 5 10 15

Cys Ile Arg Asn Ile Cys Ile Leu Ala His Val Asp His Gly Lys Thr  
 20 25 30

Ser Leu Ser Asp Ser Leu Leu Ala Thr Asn Gly Ile Ile Ser Gln Arg  
 35 40 45

Met

<210> 67

<211> 3393

<212> DNA

<213> Candida albicans

<400> 67

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 gatgggtgcag ttgttttggc cgatgtcgtc gaaggtgtct gtcacaaaac agtcaacggt 180  
 ctacgccaat gttggattga taagttgaag ccattactag ttattaacaa aattgatagg 240  
 ttaatcacag aatggaaatt gtctcccttg gaggcatacc aacacatttc cagaattata 300  
 gaacaagtaa actctgtgat tgggtcattt tttgctgggt atagactaga agatgacttg 360  
 aattggcgtg aggttggttc tgtcggggag tttatcgaga agagtgatga agacttgtat 420  
 ttcacacctg aaaagaataa tgtaatat tgcctcgcaa tagatggatg ggcattttca 480  
 gtcaatacat ttgcaaaaat atacctgaaa aaattagggg tctctcaaca agcattgtca 540  
 aaaactctct ggggagactt ttacttggat atgaaaaata aaaaaatcat ccctggtaaa 600  
 aaattgaaaa ataatagtaa cagtttgaag ccattatttg tttcgttgat tttggaccag 660  
 gtttgggctg tttatgaaaa ctgtgttatt gaaagaaatc aagacaagtt ggaaaaaatc 720  
 attgagaaat taggggcaa aatcacccct cgtgatttgc gatccaaaga ttacaagaac 780  
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 gaaacgattt atagtgcagt ggattcagaa ctggataaat ccaaactagt cgacccttca 960  
 tttgtcaagg cgatgcagga atgtgatagt tcacaccggg aaaccatac aatagcatat 1020  
 gtatcaaaat tgtgtcaat cccaatgaa gacttaccca aagctagtaa tgccgctact 1080  
 ggaggattga cggccgatga aatccaagaa cgaggaagaa ttgctcgaga attagccaaa 1140

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aaggcatctg aagcagctgc tttggcacia gaagggtcca aaaatgaaga tgagtttgcc 1200
attaaaccca agaaagatcc atttgaatgg gaatttgagg aggacgattt tgagaatgag 1260
gaagatgaga gcgatgcaaa cgcagttgaa gaatcaactg aaaccatagt gggtttcact 1320
cgtattttatt ctggatcggt atctagaggc caaaagctca cggttaattgg acccaaatac 1380
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caccgttacc tgaagataaa ccatacatta atttagcttc aacatcaacc ttgatccaca 1620
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aacgaggatt agatttattg gccaaagccg acccggtttt ggaatgggtat gtcgacgacg 1740
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tcagagaggg gttggcagat gacaaaatca gtaccaacac caataataac aacgacgaca 1920
atgaagatca tgaattagat gaaaacgaag atgagcttgc tgatttagag tttgatattt 1980
ctccgttgcc attagaagtg actcagtttt taattgagaa tgaaacgatt attgccgaaa 2040
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ctattattga taattctaatt ttggctacac aatttccaga caccaagtct tttatcaaca 2160
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3393

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&lt;210&gt; 68

&lt;211&gt; 497

&lt;212&gt; PRT

<213> *Candida albicans*

&lt;400&gt; 68

Val Met Arg Leu Gln Gln Gly Ser Gln Glu Pro Glu Val His Glu His

1

5

10

15

Leu Ile Asn Ser Ile Asp Ser Pro Gly His Ile Asp Phe Ser Ser Glu  
 20 25 30  
 Val Ser Thr Ser Ser Arg Leu Cys Asp Gly Ala Val Val Leu Val Asp  
 35 40 45  
 Val Val Glu Gly Val Cys Ser Gln Thr Val Asn Val Leu Arg Gln Cys  
 50 55 60  
 Trp Ile Asp Lys Leu Lys Pro Leu Leu Val Ile Asn Lys Ile Asp Arg  
 65 70 75 80  
 Leu Ile Thr Glu Trp Lys Leu Ser Pro Leu Glu Ala Tyr Gln His Ile  
 85 90 95  
 Ser Arg Ile Ile Glu Gln Val Asn Ser Val Ile Gly Ser Phe Phe Ala  
 100 105 110  
 Gly Asp Arg Leu Glu Asp Asp Leu Asn Trp Arg Glu Ala Gly Ser Val  
 115 120 125  
 Gly Glu Phe Ile Glu Lys Ser Asp Glu Asp Leu Tyr Phe Thr Pro Glu  
 130 135 140  
 Lys Asn Asn Val Ile Phe Ala Ser Ala Ile Asp Gly Trp Ala Phe Ser  
 145 150 155 160  
 Val Asn Thr Phe Ala Lys Ile Tyr Ser Lys Lys Leu Gly Phe Ser Gln  
 165 170 175  
 Gln Ala Leu Ser Lys Thr Leu Trp Gly Asp Phe Tyr Leu Asp Met Lys  
 180 185 190  
 Asn Lys Lys Ile Ile Pro Gly Lys Lys Leu Lys Asn Asn Ser Asn Ser  
 195 200 205  
 Leu Lys Pro Leu Phe Val Ser Leu Ile Leu Asp Gln Val Trp Ala Val  
 210 215 220  
 Tyr Glu Asn Cys Val Ile Glu Arg Asn Gln Asp Lys Leu Glu Lys Ile  
 225 230 235 240  
 Ile Glu Lys Leu Gly Ala Lys Ile Thr Pro Arg Asp Leu Arg Ser Lys  
 245 250 255  
 Asp Tyr Lys Asn Leu Leu Asn Leu Ile Met Ser Gln Trp Ile Pro Leu  
 260 265 270



Ser His Ala Ile Leu Gly Ser Val Ile Glu Tyr Leu Pro Ser Pro Ile  
 275 280 285  
 Val Ala Gln Arg Glu Arg Ile Asp Lys Ile Leu Asp Glu Thr Ile Tyr  
 290 295 300  
 Ser Ala Val Asp Ser Glu Ser Asp Lys Ser Lys Leu Val Asp Pro Ser  
 305 310 315 320  
 Phe Val Lys Ala Met Gln Glu Cys Asp Ser Ser His Pro Glu Thr His  
 325 330 335  
 Thr Ile Ala Tyr Val Ser Lys Leu Leu Ser Ile Pro Asn Glu Asp Leu  
 340 345 350  
 Pro Lys Ala Ser Asn Ala Ala Thr Gly Gly Leu Thr Ala Asp Glu Ile  
 355 360 365  
 Gln Glu Arg Gly Arg Ile Ala Arg Glu Leu Ala Lys Lys Ala Ser Glu  
 370 375 380  
 Ala Ala Ala Leu Ala Gln Glu Gly Ser Lys Asn Glu Asp Glu Phe Ala  
 385 390 395 400  
 Ile Lys Pro Lys Lys Asp Pro Phe Glu Trp Glu Phe Glu Glu Asp Asp  
 405 410 415  
 Phe Glu Asn Glu Glu Asp Glu Ser Asp Ala Asn Ala Val Glu Glu Ser  
 420 425 430  
 Thr Glu Thr Ile Val Gly Phe Thr Arg Ile Tyr Ser Gly Ser Leu Ser  
 435 440 445  
 Arg Gly Gln Lys Leu Thr Val Ile Gly Pro Lys Tyr Asp Pro Ser Leu  
 450 455 460  
 Pro Arg Asp His Gln Thr Asn Phe Glu Gln Ile Thr Asn Glu Val Glu  
 465 470 475 480  
 Ile Lys Asp Leu Phe Leu Ile Met Gly Arg Glu Leu Val Arg Met Glu  
 485 490 495  
 Lys

&lt;210&gt; 69

&lt;211&gt; 467

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 69

Pro Ala Gly Asn Ile Val Gly Val Val Gly Leu Asp Asn Ala Val Leu  
 1 5 10 15

Lys Asn Ala Thr Ile Cys Ser Pro Leu Pro Glu Asp Lys Pro Tyr Ile  
 20 25 30

Asn Leu Ala Ser Thr Ser Thr Leu Ile His Asn Lys Pro Ile Met Lys  
 35 40 45

Ile Ala Val Glu Pro Thr Asn Pro Ile Lys Leu Ala Lys Leu Glu Arg  
 50 55 60

Gly Leu Asp Leu Leu Ala Lys Ala Asp Pro Val Leu Glu Trp Tyr Val  
 65 70 75 80

Asp Asp Glu Ser Gly Glu Leu Ile Val Cys Val Ala Gly Glu Leu His  
 85 90 95

Leu Glu Arg Cys Leu Lys Asp Leu Glu Glu Arg Phe Ala Lys Gly Cys  
 100 105 110

Glu Val Thr Val Lys Glu Pro Val Ile Pro Phe Arg Glu Gly Leu Ala  
 115 120 125

Asp Asp Lys Ile Ser Thr Asn Thr Asn Asn Asn Asn Asp Asp Asn Glu  
 130 135 140

Asp His Glu Leu Asp Glu Asn Glu Asp Glu Leu Ala Asp Leu Glu Phe  
 145 150 155 160

Asp Ile Ser Pro Leu Pro Leu Glu Val Thr Gln Phe Leu Ile Glu Asn  
 165 170 175

Glu Thr Ile Ile Ala Glu Ile Val Asn Asn Lys Gln Asp Thr His Glu  
 180 185 190

Ile Arg Asn Asp Phe Ile Glu Lys Phe Ala Thr Ile Ile Asp Asn Ser  
 195 200 205

Asn Leu Ala Thr Gln Phe Pro Asp Thr Lys Ser Phe Ile Asn Asn Ile  
 210 215 220

Ile Cys Phe Gly Pro Lys Arg Val Gly Pro Asn Ile Phe Ile Glu Asp  
 225 230 235 240

Tyr Gly Leu Asn Lys Phe Arg His Leu Leu Gly Glu Ser Ala Thr Glu  
 245 250 255  
 Ser Arg Phe Val Tyr Glu Asn Asn Val Phe Asn Gly Val Gln Leu Val  
 260 265 270  
 Phe Asn Gly Gly Pro Leu Ala Ser Glu Pro Met Gln Gly Ile Ile Val  
 275 280 285  
 Arg Leu Lys Lys Ala Glu Lys Arg Glu Val Asp Glu Asp Lys Ile Val  
 290 295 300  
 Asn Pro Gly Lys Ile Ile Thr Gln Thr Arg Asp Leu Ile Tyr Lys Arg  
 305 310 315 320  
 Phe Leu Gln Lys Ser Pro Arg Leu Tyr Leu Ala Met Tyr Thr Cys Glu  
 325 330 335  
 Ile Gln Ala Ala Ala Glu Val Leu Gly Lys Val Tyr Ala Val Val Gln  
 340 345 350  
 Arg Arg Glu Gly Ser Ile Ile Ser Glu Glu Met Lys Glu Gly Thr Pro  
 355 360 365  
 Phe Phe Thr Ile Val Ala Arg Ile Pro Val Ile Glu Ala Phe Gly Phe  
 370 375 380  
 Ser Glu Asp Ile Arg Lys Lys Thr Ser Gly Ala Ala Ser Pro Gln Leu  
 385 390 395 400  
 Val Phe Asp Gly Tyr Asp Met Leu Asp Ile Asp Pro Phe Trp Val Pro  
 405 410 415  
 His Thr Glu Glu Glu Leu Glu Glu Leu Gly Glu Phe Ala Glu Arg Glu  
 420 425 430  
 Asn Val Ala Arg Arg Tyr Met Asn Asn Ile Arg Arg Arg Lys Gly Leu  
 435 440 445  
 Phe Val Asp Glu Lys Val Val Lys Asn Ala Glu Lys Gln Arg Thr Leu  
 450 455 460  
 Lys Arg Asp  
 465

&lt;210&gt; 70

&lt;211&gt; 1340

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 70

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ttattatgtg atgatatcga tgtttgtgcc aggtgtcaag gtggttaaca tgctggccac 120
acgattgttg ttggtaaagt caagtatgac ttccacatgt taccttctgg tttgggtcaat 180
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gaattggaaa acttggaagc aaaaggggta gattgtcgtg atagattggt tgtttcatct 300
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aaggcaagta gatcaggtat cagagtccac catttagtca accctgatcc agaagcttgg 480
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ccattcgtcg tcgactccgt caacttcatt cacgaagcta ttgctgcaa taaaaaaatc 660
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ttttattaga ttaataacct

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1340

&lt;210&gt; 71

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 71

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Met Cys Asp Val Val Leu Gly Ser Gln Trp Gly Asp Glu Gly Lys Gly
  1             5             10             15

Lys Leu Val Asp Leu Leu Cys Asp Asp Ile Asp Val Cys Ala Arg Cys
      20             25             30

Gln Gly Gly Asn Asn Ala Gly His Thr Ile Val Val Gly Lys Val Lys
      35             40             45

Tyr Asp Phe His Met Leu Pro Ser Gly Leu Val Asn Pro Lys Cys Gln
      50             55             60

Asn Leu Val Gly Ser Gly Val Val Ile His Val Pro Ser Phe Phe Ala

```

65                                      70                                      75                                      80  
 Glu Leu Glu Asn Leu Glu Ala Lys Gly Leu Asp Cys Arg Asp Arg Leu  
    85                                      90                                      95  
 Phe Val Ser Ser Arg Ala His Leu Val Phe Asp Phe His Gln Arg Thr  
    100                                      105                                      110  
 Asp Lys Leu Lys Glu Ala Glu Leu Ser Thr Asn Lys Lys Ser Ile Gly  
    115                                      120                                      125  
 Thr Thr Gly Lys Gly Ile Gly Pro Thr Tyr Ser Thr Lys Ala Ser Arg  
    130                                      135                                      140  
 Ser Gly Ile Arg Val His His Leu Val Asn Pro Asp Pro Glu Ala Trp  
 145                                      150                                      155                                      160  
 Glu Glu Phe Lys Thr Arg Tyr Leu Arg Leu Val Glu Ser Arg Gln Lys  
    165                                      170                                      175  
 Arg Tyr Gly Glu Phe Glu Tyr Asp Pro Lys Glu Glu Leu Ala Arg Phe  
    180                                      185                                      190  
 Glu Lys Tyr Arg Glu Thr Leu Arg Pro Phe Val Val Asp Ser Val Asn  
    195                                      200                                      205  
 Phe Met His Glu Ala Ile Ala Ala Asn Lys Lys Ile Leu Val Glu Gly  
    210                                      215                                      220  
 Ala Asn Ala Leu Met Leu Asp Ile Asp Phe Gly Thr Tyr Pro Tyr Val  
 225                                      230                                      235                                      240  
 Thr Ser Ser Ser Thr Gly Ile Gly Gly Val Leu Thr Gly Leu Gly Ile  
    245                                      250                                      255  
 Pro Pro Arg Thr Ile Arg Asn Val Tyr Gly Val Val Lys Ala Tyr Thr  
    260                                      265                                      270  
 Thr Arg Val Gly Glu Gly Pro Phe Pro Thr Glu Gln Leu Asn Lys Val  
    275                                      280                                      285  
 Gly Glu Thr Leu Gln Asp Val Gly Ala Glu Tyr Gly Val Thr Thr Gly  
    290                                      295                                      300  
 Arg Lys Arg Arg Cys Gly Trp Leu Asp Leu Val Val Leu Lys Tyr Ser  
 305                                      310                                      315                                      320  
 Asn Ser Ile Asn Gly Tyr Thr Ser Leu Asn Ile Thr Lys Leu Asp Val

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aaaatatatg	gtattttctta	tgattcaatg	aatactggtg	ctgggggtatt	atttatattt	360
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caagtccaac	aatcattaac	tgattttatt	ttggctcatg	aattgggtac	agcattaaca	600
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gctcaagctc	aaactttccg	gtgggtcggg	tggtgggggtg	ccatttatatg	tggtgccact	720
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aaccacactta	caaataatat	cattcctcac	gagaagaaaa	attcaatgga	acaagaatta	900
tctcatgaat	atatcactgc	aaacaataat	gaacatgacg	ttgttccaat	tgatcctgaa	960
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tcacatttac	cagcagtttg	gttttcggga	ttattatggg	ggttacaaga	tactttatatg	1140
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<210> 73

<211> 584

<212> PRT

<213> Candida albicans

<400> 73

Met Ala Phe Asp Thr Thr Val Pro Gln Glu Tyr Tyr Asp Glu Asn Phe  
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Ile Pro Gly Thr Thr Asn Ile Leu Thr Gly Lys Thr Thr Ile Asp Glu  
 20 25 30

Ser Ser Ser Ile Thr Thr Gln Lys Ser Leu Lys Arg Asp Pro Lys Thr  
 35 40 45

Gly Leu Val Leu Met Pro Gln Pro Thr Ser Ser Pro Asn Asp Pro Leu  
 50 55 60

Asn Trp Ser Pro Phe Arg Lys Phe Ala Gln Leu Thr Leu Leu Ser Phe  
 65 70 75 80

Ile Thr Ala Leu Thr Ala Ala Thr Ser Asn Asp Ala Gly Ala Thr Gln  
 85 90 95

Asp Ser Leu Asn Lys Ile Tyr Gly Ile Ser Tyr Asp Ser Met Asn Thr  
 100 105 110

Gly Ala Gly Val Leu Phe Ile Phe Ile Gly Trp Ser Cys Met Phe Phe  
 115 120 125

Ala Pro Ala Ser Ser Leu Tyr Gly Arg Arg Ile Thr Tyr Ile Ile Cys  
 130 135 140

Leu Leu Ala Gly Thr Leu Gly Cys Val Trp Phe Ala Leu Ser Lys Arg  
 145 150 155 160

Thr Ala Asp Thr Ile Trp Ser Gln Ala Phe Val Gly Met Ser Glu Ala  
 165 170 175  
 Cys Ala Glu Ala Gln Val Gln Gln Ser Leu Thr Asp Leu Phe Leu Ala  
 180 185 190  
 His Glu Leu Gly Thr Ala Leu Thr Ile Tyr Ile Ser Ala Thr Ser Ile  
 195 200 205  
 Gly Thr Leu Leu Gly Pro Leu Ile Ala Gln Asp Ile Ala Gln Ala Gln  
 210 215 220  
 Thr Phe Arg Trp Val Gly Trp Trp Gly Ala Ile Ile Cys Gly Ala Thr  
 225 230 235 240  
 Leu Ile Val Ile Ile Phe Gly Cys Glu Glu Thr Val Phe Asp Arg Gln  
 245 250 255  
 Leu Tyr Thr Lys Val Leu Glu Ser Glu Asn Val Thr Gln Ile Pro Asp  
 260 265 270  
 Pro Ser Glu Glu Lys Lys Gln Asp Asn Pro Leu Thr Asn Asn Ile Ile  
 275 280 285  
 Pro His Glu Lys Lys Asn Ser Met Glu Gln Glu Leu Ser His Glu Tyr  
 290 295 300  
 Ile Thr Ala Asn Asn Asn Glu His Asp Val Val Pro Ile Asp Pro Glu  
 305 310 315 320  
 Thr Leu Asn Glu Lys Lys Lys Ser Tyr Trp Gln Arg Ile Ala Ile Ile  
 325 330 335  
 Thr Pro Ala Pro Tyr Leu Gln Gly Leu Gly Phe Lys Gln Tyr Leu Glu  
 340 345 350  
 Arg Phe Ile Ile Tyr Phe Lys Ile Phe Thr Leu Pro Ala Val Trp Phe  
 355 360 365  
 Ser Gly Leu Leu Trp Gly Leu Gln Asp Thr Tyr Met Thr Phe Phe Leu  
 370 375 380  
 Thr Thr Gln Asp Thr Tyr Phe Tyr Asn Pro Pro Trp Asn Lys Ser Asn  
 385 390 395 400  
 Ala Gly Val Ala Ile Met Asn Val Ala Thr Leu Ile Gly Ala Val Ile  
 405 410 415



Gly Cys Ile Val Ser Gly Leu Phe Ser Asp Tyr His Val Ile Trp L u  
420 425 430

Ala Lys Arg Asn Asn Gly Ile Met Glu Ala Glu Tyr Arg Leu Tyr Leu  
435 440 445

Leu Val Ile Thr Leu Ile Ile Ser Pro Val Gly Leu Ile Met Phe Gly  
450 455 460

Val Gly Ala Ala Arg Glu Trp Pro Trp Gln Val Ile Tyr Val Gly Leu  
465 470 475 480

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<210> 75

<211> 331

<212> PRT

<213> Candida albicans

<400> 75

Met Ser Gly Pro Val Asn Ser Val Ser Lys Gln Met Asn Val Asp Thr  
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Asp Ile Ile Thr Leu Thr Arg Phe Ile Leu Gln Glu Gln Gln Thr Val  
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Ala Pro Thr Ala Thr Gly Glu Leu Ser Leu Leu Leu Asn Ala Leu Gln  
 35 40 45

Phe Ala Phe Lys Phe Ile Ala His Asn Ile Arg Arg Ala Glu Leu Val  
 50 55 60

Asn Leu Ile Gly Val Ser Gly Ser Ala Asn Ser Thr Gly Asp Val Gln  
 65 70 75 80

Lys Lys Leu Asp Val Ile Gly Asp Glu Ile Phe Ile Asn Ala Met Arg  
 85 90 95

Ser Ser Asn Asn Val Lys Val Leu Val Ser Glu Glu Gln Glu Asp Leu  
 100 105 110

Ile Val Phe Pro Gly Gly Gly Thr Tyr Ala Val Cys Thr Asp Pro Ile  
 115 120 125

Asp Gly Ser Ser Asn Ile Asp Ala Gly Val Ser Val Gly Thr Ile Phe  
 130 135 140

Gly Val Tyr Lys Leu Gln Glu Gly Ser Thr Gly Gly Ile Ser Asp Val  
 145 150 155 160

Leu Arg Pro Gly Lys Glu Met Val Ala Ala Gly Tyr Thr Met Tyr Gly

165 170 175

Ala Ser Ala His Leu Ala Leu Thr Thr Gly His Gly Val Asn Leu Phe  
180 185 190

Thr Leu Asp Thr Gln Leu Gly Glu Phe Ile Leu Thr His Pro Asn Leu  
195 200 205

Lys Leu Pro Asp Thr Lys Asn Ile Tyr Ser Leu Asn Glu Gly Tyr Ser  
210 215 220

Asn Lys Phe Pro Glu Tyr Val Gln Asp Tyr Ser Lys Asp Ile Lys Lys  
225 230 235 240

Glu Gly Tyr Ser Leu Arg Tyr Ile Gly Ser Met Val Ala Asp Val His  
245 250 255

Arg Thr Leu Leu Tyr Gly Gly Ile Phe Ala Tyr Pro Thr Leu Lys Leu  
260 265 270

Arg Val Leu Tyr Glu Cys Phe Pro Met Ala Leu Leu Met Glu Gln Ala  
275 280 285

Gly Gly Ser Ala Val Thr Ile Lys Gly Glu Arg Ile Leu Asp Ile Leu  
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Pro Lys Gly Ile His Asp Lys Ser Ser Ile Val Leu Gly Ser Lys Gly  
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Glu Val Glu Lys Tyr Leu Lys His Val Pro Lys  
325 330

<210> 76  
<211> 1686  
<212> DNA  
<213> Candida albicans

<400> 76

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 gatcattcat taaattatca tttttatcga gcattaaaaa aatcattata taaaccagga 1200  
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 gaaaaaacca ccaaagtcaa taatggtcct caattaccag tggtatggca taaagcattc 1560  
 ttatcatttg ctactcgta taaaaatgat cttactgatg atcaaaaaga tttcttatta 1620  
 gaaacagtaa gacaaagatt tcacctccta attggtcctg aaattcgtag agaattacta 1680  
 agttag 1686

&lt;210&gt; 77

&lt;211&gt; 475

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 77

Met Gly Lys Ile Thr Thr Ser Asp Thr Lys Thr Lys Gln Arg His Asn  
 1 5 10 15

Pro Leu Leu Lys Asp Ile Ser Ser Gln Gly Gly Asn Leu Arg Thr Val  
 20 25 30

Pro Arg Ser Ser Ser Ser Ser Ser Gln Lys Lys Lys Ser Ser Lys  
 35 40 45

Lys Gln Arg His Asn Asp Glu Asp Asp Glu Glu Asn Gly Gly Gly Glu  
 50 55 60

Gly Phe Leu Asp Ala Ser Ser Ser Arg Lys Ile Leu Gln Leu Ala Lys  
 65 70 75 80

Glu Gln Gln Asp Glu Leu Glu Gln Glu Asp Glu Ile Gln Asn Lys Pro  
 85 90 95

Ser Phe Ala Gln Ser Phe Lys Asn Gln Gln Ile Asp Ser Glu Glu Glu  
 100 105 110

Glu Glu Glu Asp Glu Tyr Ser Asp Phe Glu Glu Glu Glu Glu Val Glu  
 115 120 125  
 Glu Ile Val Tyr Asp Glu Glu Asp Ala Glu Val Asp Pro Lys Asp Ala  
 130 135 140  
 Glu Leu Phe Asn Lys Tyr Phe Gln Ser Asn Gly Glu Ala Asn Asn Asn  
 145 150 155 160  
 Asp Asp Asp Asn Ser Phe Gln Pro Thr Ile Asn Leu Ala Asp Lys Ile  
 165 170 175  
 Leu Ala Lys Ile Gln Glu Lys Glu Ser Gln Gln Gln Gln Gln Gln  
 180 185 190  
 Ser Ser Pro Asp Asn Ser Asn Glu Asp Ala Val Leu Leu Pro Pro Lys  
 195 200 205  
 Val Ile Leu Ala Tyr Glu Lys Ile Gly Gln Ile Leu Ser Thr Tyr Thr  
 210 215 220  
 His Gly Lys Leu Pro Lys Leu Phe Lys Ile Leu Pro Ser Leu Lys Asn  
 225 230 235 240  
 Trp Gln Asp Val Leu Tyr Val Thr Asn Pro Asn Ser Trp Thr Pro His  
 245 250 255  
 Ala Thr Tyr Glu Ala Thr Lys Leu Phe Val Ser Asn Leu Ser Ser Asn  
 260 265 270  
 Glu Ala Thr Val Phe Ile Glu Thr Ile Leu Leu Pro Arg Phe Arg Asp  
 275 280 285  
 Ser Ile Glu Asn Ser Asp Asp His Ser Leu Asn Tyr His Ile Tyr Arg  
 290 295 300  
 Ala Leu Lys Lys Ser Leu Tyr Lys Pro Gly Ala Phe Phe Lys Gly Phe  
 305 310 315 320  
 Leu Leu Pro Leu Val Asp Gly Tyr Cys Ser Val Arg Glu Ala Thr Ile  
 325 330 335  
 Ala Ala Ser Val Leu Thr Lys Val Ser Val Pro Val Leu His Ser Ser  
 340 345 350  
 Val Ala Leu Thr Gln Leu Leu Thr Arg Asp Phe Asn Pro Ala Thr Thr  
 355 360 365

Val Phe Ile Arg Val Leu Ile Glu Lys Lys Tyr Ala Leu Pro Tyr Gln  
 370 375 380

Thr Leu Asp Glu Leu Val Phe Tyr Phe Met Arg Phe Arg Asn Ala Thr  
 385 390 395 400

Ile Asn Gln Asp Glu Asn Met Glu Asn Met Asp Ile Asp Gln Glu Lys  
 405 410 415

Thr Thr Lys Val Asn Asn Gly Pro Gln Leu Pro Val Val Trp His Lys  
 420 425 430

Ala Phe Leu Ser Phe Ala Thr Arg Tyr Lys Asn Asp Leu Thr Asp Asp  
 435 440 445

Gln Lys Asp Phe Leu Leu Glu Thr Val Arg Gln Arg Phe His Pro Leu  
 450 455 460

Ile Gly Pro Glu Ile Arg Arg Glu Leu Leu Ser  
 465 470 475

&lt;210&gt; 78

&lt;211&gt; 1519

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 78

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 ctccgcccc tcttttcat atactatctc ccttcttct tcttctctt tttattttt 180  
 caattattac aatcttatgt catttaaagg attcaaaaag ggtgtcctta gggccccaca 240  
 gacaatgcgt cagaaattca acatgggaga aatcacccaa gatgctgtt atctcgatgc 300  
 tgaaagaaga ttcaaagaaa tcgaaacgga aacaaaaaag ttgagtgaag aatccaagaa 360  
 atatttcaat gctgtcaatg ggatgttaga tgaacaaatt gattttgcc aagccgtggc 420  
 tgagatttat aaaccaatca gtggttagatt atcggacccc agtgctacgg taccagaaga 480  
 taaccacaaa ggtattgaag catcggaact gtaccaagca gtgggttaaag atctcaaaga 540  
 taccttaaaa cccgatttgg aattgattga aaaaagaatt gttgaaccag cacaagaatt 600  
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 tttggatcgt cataagagaa atttttctaa atatgaactg aagaaagaaa gaactgttaa 720  
 agatgaagaa aaaaatgttca gtgctcaagc agaagtagaa attgctcaac aagagtacga 780  
 ttattataat gatttgtaa agaattgaatt gccagttttg tttcaaagc aaagtattt 840  
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 cactagaatg gaagagttga aaattccata ttttgatttg tctactgata ttgtcgaagc 960  
 ttatactgcc aagaagggga acattgagga acaaaccgat gctattggaa tcaactattt 1020  
 caaagtcggg catgccaaat ccaaattgga agccactaaa agaagacatg ctgctatgaa 1080  
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 tgcatactcc ccaggaggtt acaaccaacc atatggtgat agcaagtatc ~~aaaccaacc~~ 1200

ttctccagca acataccaat ctccagtagt agcagccact gctcaatctc cagctactta 1260  
 tcaatcgcca gtggctactg gacaacctcc atcatattta ccacaaactc cagccagtgc 1320  
 tccaccacca caagttggta gtggccttcc aacatgcacg gctttatacg attatactgc 1380  
 acaagcccag ggtgacttga cttccctgc aggagctgtt attgaaatta tacaagaac 1440  
 cgaagatgcc aacggatggt ggactggtaa atacaatggt caaacgggtg tgttcctgg 1500  
 taattatgtg caattatag 1519

<210> 79

<211> 440

<212> PRT

<213> Candida albicans

<400> 79

Met Ser Phe Lys Gly Phe Lys Lys Gly Val Leu Arg Ala Pro Gln Thr  
 1 5 10 15  
 Met Arg Gln Lys Phe Asn Met Gly Glu Ile Thr Gln Asp Ala Val Tyr  
 20 25 30  
 Leu Asp Ala Glu Arg Arg Phe Lys Glu Ile Glu Thr Glu Thr Lys Lys  
 35 40 45  
 Leu Ser Glu Glu Ser Lys Lys Tyr Phe Asn Ala Val Asn Gly Met Leu  
 50 55 60  
 Asp Glu Gln Ile Asp Phe Ala Lys Ala Val Ala Glu Ile Tyr Lys Pro  
 65 70 75 80  
 Ile Ser Gly Arg Leu Ser Asp Pro Ser Ala Thr Val Pro Glu Asp Asn  
 85 90 95  
 Pro Gln Gly Ile Glu Ala Ser Glu Ser Tyr Gln Ala Val Val Lys Asp  
 100 105 110  
 Leu Lys Asp Thr Leu Lys Pro Asp Leu Glu Leu Ile Glu Lys Arg Ile  
 115 120 125  
 Val Glu Pro Ala Gln Glu Leu Leu Lys Ile Ile Gln Ala Ile Arg Lys  
 130 135 140  
 Met Ser Val Lys Arg Asp His Lys Gln Leu Asp Leu Asp Arg His Lys  
 145 150 155 160  
 Arg Asn Phe Ser Lys Tyr Glu Ser Lys Lys Glu Arg Thr Val Lys Asp  
 165 170 175  
 Glu Glu Lys Met Phe Ser Ala Gln Ala Glu Val Glu Ile Ala Gln Gln  
 180 185 190

Glu Tyr Asp Tyr Tyr Asn Asp Leu Leu Lys Asn Glu Leu Pro Val Leu  
 195 200 205  
 Phe Gln Met Gln Ser Asp Phe Ile Lys Pro Leu Phe Val Ser Phe Tyr  
 210 215 220  
 Tyr Met Gln Leu Asn Ile Phe Tyr Thr Leu Tyr Thr Arg Met Glu Glu  
 225 230 235 240  
 Leu Lys Ile Pro Tyr Phe Asp Leu Ser Thr Asp Ile Val Glu Ala Tyr  
 245 250 255  
 Thr Ala Lys Lys Gly Asn Ile Glu Glu Gln Thr Asp Ala Ile Gly Ile  
 260 265 270  
 Thr His Phe Lys Val Gly His Ala Lys Ser Lys Leu Glu Ala Thr Lys  
 275 280 285  
 Arg Arg His Ala Ala Met Asn Ser Pro Pro Pro Thr Gly Ala Ser Ser  
 290 295 300  
 Ile Ala Ser Thr Gly Thr Gly Gly Glu Leu Pro Ala Tyr Ser Pro Gly  
 305 310 315 320  
 Gly Tyr Asn Gln Pro Tyr Gly Asp Ser Lys Tyr Gln Pro Pro Ser Ser  
 325 330 335  
 Pro Ala Thr Tyr Gln Ser Pro Val Val Ala Ala Thr Ala Gln Ser Pro  
 340 345 350  
 Ala Thr Tyr Gln Ser Pro Val Ala Thr Gly Gln Pro Pro Ser Tyr Leu  
 355 360 365  
 Pro Gln Thr Pro Ala Ser Ala Pro Pro Pro Gln Val Gly Ser Gly Leu  
 370 375 380  
 Pro Thr Cys Thr Ala Leu Tyr Asp Tyr Thr Ala Gln Ala Gln Gly Asp  
 385 390 395 400  
 Leu Thr Phe Pro Ala Gly Ala Val Ile Glu Ile Ile Gln Arg Thr Glu  
 405 410 415  
 Asp Ala Asn Gly Trp Trp Thr Gly Lys Tyr Asn Gly Gln Thr Gly Val  
 420 425 430  
 Phe Pro Gly Asn Tyr Val Gln Leu  
 435 440



<210> 80  
 <211> 861  
 <212> DNA  
 <213> *Candida albicans*

<400> 80  
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 ggtcccgta aatcaatcaa tatgccaaag gatcgtatat tgaaaacaca ccaggggtat 180  
 ggatttgcg aatttaaaaa ctcagcagat gccaaatata ctatggaaat actacgagga 240  
 ataagacttt atggaaaagc attgaaattg aaacgaattg atgccaagtc tcagtcatca 300  
 acaaacacc caaataatca aacaatagga acatttgtac aatcagattt gatcaatcca 360  
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 tcctttttta tggatacgtt tagtaagttt ggaacccctta taagaaaccc aataattaga 480  
 cgtgattcag agggacactc tttgggatac ggatttctta cgtacgatga ctttgaaagt 540  
 agtgatttat gcatacaaaa aatgaacaac acgattttga tgaataacaa aattgctatc 600  
 agttatgcat tcaaggatct gagtgttgat ggaagaaat cccggcatgg agatcaagtg 660  
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 gcaggtacga cgaagggaaa taaaaggag aataaaccac ataaagtac caaacgtga 780  
 gacaatgagt tagtcccccc tttcaaaata agtagagtat caccatagtt tatgaaacaa 840  
 ttgatattt aagcttctct g 861

<210> 81  
 <211> 1641  
 <212> DNA  
 <213> *Candida albicans*

<400> 81  
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 agtgcataca ttggtatcat cattatgtgt ttccttattg cctttgggtg ttttgttttc 180  
 ggtttcgata ctggtaccat ttctggtttt attaatatgt ctgacttttt agaaagattc 240  
 ggtggtacta aagctgacgg tactctttac ttttccaatg tcagaactgg tgtaattgatt 300  
 ggtttgttca acgctgggtg tgccattggg gcattattct tgtctaaagt cgggtgatatg 360  
 tatggtagaa gagttggtat catgactgct atgattgtct atattgttgg tattattggt 420  
 caaattgctt ctcaacatgc ttggtatcaa gtcattgatt gtagaattat cactggtctt 480  
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 aacaagggtt ctccagagga ccagcatta taccgtgaac ttcaattaat ccaagctggt 840  
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 agaattcttg aaagagttat tgttgggtgc atgttacaag ctttacaaca attaaactgg 960  
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gctattgaaa gaatgggtag aagactctgt ttgttaactg gttccgttgc catgtcaatc 1140  
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 ccagaagagg aacacgttta a 1641

&lt;210&gt; 82

&lt;211&gt; 546

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 82

Met Ser Gln Asp Asn Val Ser Ser Thr Ser Thr Ala Glu Ala Val Asn  
 1 5 10 15

Asn Glu Ile Lys Val Lys Asp Glu Phe Pro Gln Glu Glu Gln Ala His  
 20 25 30

Thr Ser Leu Glu Asp Lys Pro Val Ser Ala Tyr Ile Gly Ile Ile Ile  
 35 40 45

Met Cys Phe Leu Ile Ala Phe Gly Gly Phe Val Phe Gly Phe Asp Thr  
 50 55 60

Gly Thr Ile Ser Gly Phe Ile Asn Met Ser Asp Phe Leu Glu Arg Phe  
 65 70 75 80

Gly Gly Thr Lys Ala Asp Gly Thr Leu Tyr Phe Ser Asn Val Arg Thr  
 85 90 95

Gly Val Met Ile Gly Leu Phe Asn Ala Gly Gly Ala Ile Gly Ala Leu  
 100 105 110

Phe Leu Ser Lys Val Gly Asp Met Tyr Gly Arg Arg Val Gly Ile Met  
 115 120 125

Thr Ala Met Ile Val Tyr Ile Val Gly Ile Ile Val Gln Ile Ala Ser  
 130 135 140

Gln His Ala Trp Tyr Gln Val Met Ile Gly Arg Ile Ile Thr Gly Leu  
 145 150 155 160

Ala Val Gly Met Leu Ser Val Leu Cys Bro Leu Phe Ile Ser Glu Val

165	170	175
Ser Pro Lys His Leu Arg Gly Thr Leu Val Cys Cys Phe Gln Leu Met		
180	185	190
Ile Thr Leu Gly Ile Phe Leu Gly Tyr Cys Thr Thr Tyr Gly Thr Lys		
195	200	205
Ser Tyr Ser Asp Ser Arg Gln Trp Arg Ile Pro Leu Gly Leu Cys Phe		
210	215	220
Ala Trp Ala Leu Cys Leu Val Ala Gly Met Val Arg Met Pro Glu Ser		
225	230	235 240
Pro Arg Tyr Leu Val Gly Lys Asp Arg Ile Glu Asp Ala Lys Met Ser		
245	250	255
Leu Ala Lys Thr Asn Lys Val Ser Pro Glu Asp Pro Ala Leu Tyr Arg		
260	265	270
Glu Leu Gln Leu Ile Gln Ala Gly Val Glu Arg Glu Arg Leu Ala Gly		
275	280	285
Lys Ala Ser Trp Gly Thr Leu Phe Asn Gly Lys Pro Arg Ile Phe Glu		
290	295	300
Arg Val Ile Val Gly Val Met Leu Gln Ala Leu Gln Gln Leu Thr Gly		
305	310	315 320
Asp Asn Tyr Phe Phe Tyr Tyr Ser Thr Thr Ile Phe Lys Ser Val Gly		
325	330	335
Met Asn Asp Ser Phe Glu Thr Ser Ile Ile Ile Gly Val Ile Asn Phe		
340	345	350
Ala Ser Thr Phe Val Gly Ile Tyr Ala Ile Glu Arg Met Gly Arg Arg		
355	360	365
Leu Cys Leu Leu Thr Gly Ser Val Ala Met Ser Ile Cys Phe Leu Ile		
370	375	380
Tyr Ser Leu Val Gly Thr Gln His Leu Tyr Ile Asp Lys Pro Gly Gly		
385	390	395 400
Ala Ser Arg Lys Pro Asp Gly Asp Ala Met Ile Phe Met Thr Pro Leu		
405	410	415
Tyr Val Ile Phe Ser Pro Ser Thr Trp Ala Gly Glu Val Tyr Ser Ile		

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<210> 83
<211> 1014
<212> DNA
<213> Candida albicans
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tctgaagctc	cagctaagaa	agaagaagcc	cctgaaaagg	ctaagaaga	atctgctcaa	180
gctgccgcac	caaagaagga	agaaactaag	aaagaggaac	caaagaagga	atcaaaacca	240
gctccaaaga	aagaagaatc	taagaagtc	acccaatcta	caactagtgc	tccaactttc	300
accaattttct	ccagaaacga	agagagagtt	aagatgaaca	gaatgagatt	gagaattgct	360
gaacgtctta	aggaatcaca	aaacactgct	gcttccttga	ccactttcaa	cgaagttgat	420
atgtctaaact	tgatggattt	cagaaagaaa	tacaaggacg	aatttattga	aaagaccggt	480
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ccagctgtca	atgctgcaat	tgaaaacaat	gacactttgg	tctttaaaga	ttatgccgac	600
atttcaattg	ctgttgccac	tccaaaagg	ttggtgaccc	ctgttgtcag	aaacgccgaa	660
tccttatcta	ttttgggtat	tgaaaaggaa	atctctaatt	tgggtaagaa	agccagagat	720
ggtaaattga	ctttggaaga	tatgaccggt	ggtactttca	ctatttctaa	tgggtggtgt	780
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cacggtgtta	aagaagaacc	agtataagtc	aacggacaaa	tcgtttctag	accaatgatg	900

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<210> 84

<211> 337

<212> PRT

<213> Candida albicans

<400> 84

Asn Ala Pro Val Ser Gly Thr Ile Thr Glu Phe Leu Val Asp Val Asp  
 1 5 10 15

Ala Thr Val Glu Val Gly Gln Glu Ile Ile Lys Met Glu Glu Gly Asp  
 20 25 30

Ala Pro Ala Gly Gly Ala Ser Ala Ser Glu Ala Pro Ala Lys Lys Glu  
 35 40 45

Glu Ala Pro Glu Lys Ala Lys Glu Glu Ser Ala Gln Ala Ala Ala Pro  
 50 55 60

Lys Lys Glu Glu Thr Lys Lys Glu Glu Pro Lys Lys Glu Ser Lys Pro  
 65 70 75 80

Ala Pro Lys Lys Glu Glu Ser Lys Lys Ser Thr Gln Ser Thr Thr Ser  
 85 90 95

Ala Pro Thr Phe Thr Asn Phe Ser Arg Asn Glu Glu Arg Val Lys Met  
 100 105 110

Asn Arg Met Arg Leu Arg Ile Ala Glu Arg Leu Lys Glu Ser Gln Asn  
 115 120 125

Thr Ala Ala Ser Leu Thr Thr Phe Asn Glu Val Asp Met Ser Asn Leu  
 130 135 140

Met Asp Phe Arg Lys Lys Tyr Lys Asp Glu Phe Ile Glu Lys Thr Gly  
 145 150 155 160

Ile Lys Leu Gly Phe Met Gly Ala Phe Ser Lys Ala Ser Ala Leu Ala  
 165 170 175

Leu Lys Glu Ile Pro Ala Val Asn Ala Ala Ile Glu Asn Asn Asp Thr  
 180 185 190

Leu Val Phe Lys Asp Tyr Ala Asp Ile Ser Ile Ala Val Ala Thr Pro  
 195 200 205

Lys Gly Leu Val Thr Pro Val Val Arg Asn Ala Glu Ser Leu Ser Ile  
 210 215 220  
 Leu Gly Ile Glu Lys Glu Ile Ser Asn Leu Gly Lys Lys Ala Arg Asp  
 225 230 235 240  
 Gly Lys Leu Thr Leu Glu Asp Met Thr Gly Gly Thr Phe Thr Ile Ser  
 245 250 255  
 Asn Gly Gly Val Phe Gly Ser Leu Tyr Gly Thr Pro Ile Ile Asn Met  
 260 265 270  
 Pro Gln Thr Ala Val Leu Gly Leu His Gly Val Lys Glu Arg Pro Val  
 275 280 285  
 Thr Val Asn Gly Gln Ile Val Ser Arg Pro Met Met Tyr Leu Ala Leu  
 290 295 300  
 Thr Tyr Asp His Arg Val Val Asp Gly Arg Glu Ala Val Ile Phe Leu  
 305 310 315 320  
 Arg Thr Ile Lys Glu Leu Ile Glu Asp Pro Arg Lys Met Leu Leu Leu  
 325 330 335  
 Glu

<210> 85  
 <211> 1806  
 <212> DNA  
 <213> Candida albicans

<400> 85  
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 tagccaatta ttttgacaaa ttgcatgcgg ttgaatcttt gaaatacacc attgctaacc 1440  
 caactccaaa ggacaatgtt gaaaaattgt caagaaaatt agctagatta gaaaagaatt 1500  
 tacctcattt catttacaac taccaagggt ctttggttta cattgggtct gaaaaggctg 1560  
 ttgctgattt ggtctgggtt gattgggtcaa atataagttc cggaggtaat ttgacctttt 1620  
 tattctggag atcagcttat atttacatgt gtttatcagt caagaaccaa gtgctagttg 1680  
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 agccgt 1806

&lt;210&gt; 86

&lt;211&gt; 574

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 86

Met Phe Thr Arg Ser Leu Ile Lys Gly Gly Gly Arg Leu Ala Thr Thr  
 1 5 10 15

Arg Ser Leu Val Asn Asn Ser Thr Ser Leu Val Leu Lys Asn Gln Phe  
 20 25 30

Lys Lys Tyr Ser Thr Ser Thr Pro Pro Lys Val Ala Lys Ser Lys Ser  
 35 40 45

Ser Thr Ile Gly Lys Ile Phe Arg Tyr Thr Phe Tyr Thr Ala Val Ile  
 50 55 60

Ser Val Ile Gly Ser Ala Gly Leu Ile Gly Tyr Lys Ile Tyr Glu Glu  
 65 70 75 80

Ser Gln Pro Val Asp Gln Val Lys Gln Thr Pro Leu Phe Pro Asn Gly  
 85 90 95

Glu Lys Lys Lys Thr Leu Val Ile Leu Gly Ser Gly Trp Gly Ala Ile  
 100 105 110

Ser Leu Leu Lys Asn Leu Asp Thr Thr Leu Tyr Asn Val Val Ile Val  
 115 120 125

Ser Pro Arg Asn Tyr Phe Leu Phe Thr Pro Leu Leu Pro Ser Val Pro  
 130 135 140

Thr Gly Thr Val Glu Leu Arg Ser Ile Ile Glu Pro Val Arg Ser Val  
 145 150 155 160

Thr Arg Arg Cys Pro Gly Gln Val Ile Tyr Leu Glu Ala Glu Ala Thr  
 165 170 175

Asn Ile Asn Pro Lys Thr Asn Glu Leu Thr Leu Lys Gln Ser Thr Thr  
 180 185 190

Val Val Ser Gly His Ser Gly Lys Asp Thr Ser Ser Ser Lys Ser Thr  
 195 200 205

Val Ala Glu Tyr Thr Gly Val Glu Glu Ile Thr Thr Thr Leu Asn Tyr  
 210 215 220

Asp Tyr Leu Val Val Gly Val Gly Ala Gln Pro Ser Thr Phe Gly Ile  
 225 230 235 240

Pro Gly Val Ala Glu Asn Ser Thr Phe Leu Lys Glu Val Ser Asp Ala  
 245 250 255

Ser Ala Ile Arg Arg Lys Leu Met Asp Val Ile Glu Ala Ala Asn Ile  
 260 265 270

Leu Pro Lys Asp Asp Pro Glu Arg Lys Arg Leu Leu Ser Ile Val Val  
 275 280 285

Cys Gly Gly Gly Pro Thr Gly Val Glu Ala Ala Gly Glu Ile Gln Asp  
 290 295 300

Tyr Ile Asp Gln Asp Leu Lys Lys Trp Val Pro Glu Val Ala Asp Glu  
 305 310 315 320

Leu Lys Val Ser Leu Val Glu Ala Leu Pro Asn Val Leu Asn Thr Phe  
 325 330 335

Asn Lys Lys Leu Ile Asp Tyr Thr Lys Glu Val Phe Lys Asp Thr Asn  
 340 345 350

Ile Asn Leu Met Thr Asn Thr Met Ile Lys Lys Val Asn Asp Lys Ser  
 355 360 365

Leu Ile Ala Asn His Lys Asn Pro Asp Gly Ser Thr Glu Ser Ile Glu  
 370 375 380



Ile Pro Tyr Gly Leu Leu Ile Trp Ala Thr Gly Asn Ala Pro Arg Asp  
 385 390 395 400  
 Phe Thr Arg Asp Leu Ile Ala Lys Val Asp Glu Gln Lys Asn Ala Arg  
 405 410 415  
 Arg Gly Leu Leu Val Asp Glu Arg Leu Lys Val Asp Gly Thr Asp Asn  
 420 425 430  
 Ile Phe Ala Leu Gly Asp Cys Thr Phe Thr Lys Tyr Pro Pro Thr Ala  
 435 440 445  
 Gln Val Ala Phe Gln Glu Gly Glu Tyr Leu Ala Asn Tyr Phe Asp Lys  
 450 455 460  
 Leu His Ala Val Glu Ser Leu Lys Tyr Thr Ile Ala Asn Pro Thr Pro  
 465 470 475 480  
 Lys Asp Asn Val Glu Lys Leu Ser Arg Lys Leu Ala Arg Leu Glu Lys  
 485 490 495  
 Asn Leu Pro His Phe Ile Tyr Asn Tyr Gln Gly Ser Leu Ala Tyr Ile  
 500 505 510  
 Gly Ser Glu Lys Ala Val Ala Asp Leu Val Trp Gly Asp Trp Ser Asn  
 515 520 525  
 Ile Ser Ser Gly Gly Asn Leu Thr Phe Leu Phe Trp Arg Ser Ala Tyr  
 530 535 540  
 Ile Tyr Met Cys Leu Ser Val Lys Asn Gln Val Leu Val Val Leu Asp  
 545 550 555 560  
 Trp Ala Lys Val Tyr Phe Phe Gly Arg Asp Cys Ser Lys Glu  
 565 570

&lt;210&gt; 87

&lt;211&gt; 1137

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 87

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 aatagatgtc cgctttgtaa aacagagggtt tttgaaagtg gtctaaaacg tgatccattg 240  
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 gagcagacta ctgaagttat tctgttgcta tctgatgatg aagagaatgg ttctgatagc 540  
 ctagtaaaat gtcctatttg ttttgagaga atggaattag atgtactaca gggaaagcat 600  
 attgacgact gtctaagtgg aaagagcacg aagaggacgc ctacagacat tttatcccca 660  
 aaagccaaac gaccgaagca aatcacctcc tttttcaaac caacaataga tactaaaacg 720  
 ccttcgccac ctacaagtaa ggcgtcaaca actccaacag caactccgac aactacattg 780  
 ttgaaagcaa acgtcgcac tccatcccca gtggcgcaaa gtacagttca caagggcaag 840  
 ccattaccta aactcgattt cagcagcttg agtactcaaa aaattaaagc caagttgagt 900  
 gatttgaaac taccacaac aggtagtagg aatgaaatgg aagccagata cttgcattac 960  
 tacgtgattt ataatgccaa ccttgattcc aatcatcctg taaaggaatc tattttgcga 1020  
 caacagttga aacaatggga aatggtgcaa catcaaccgt cgtttggtga tgcagagtgg 1080  
 aaaggagctg aaactgggaa ttggaaagaa ctcattgcaa gagcacggag taactaa 1137

&lt;210&gt; 88

&lt;211&gt; 378

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 88

Met Asn Leu Lys Asp Ile Thr Asp Pro Ser Asp Phe Lys Thr Thr Lys  
 1 5 10 15

Leu Pro Ala Leu Ala Glu Leu Asp Ile Leu Lys Arg Cys Tyr Ile Cys  
 20 25 30

Lys Asp Leu Leu Asn Ala Pro Val Arg Thr Gln Cys Asp His Thr Tyr  
 35 40 45

Cys Ser Gln Cys Ile Arg Glu Phe Leu Leu Arg Asp Asn Arg Cys Pro  
 50 55 60

Leu Cys Lys Thr Glu Val Phe Glu Ser Gly Leu Lys Arg Asp Pro Leu  
 65 70 75 80

Leu Glu Glu Ile Val Val Ser Tyr Ala Ser Leu Arg Pro His Leu Leu  
 85 90 95

Arg Leu Leu Glu Ile Glu Lys Val Glu Ser Lys Gln Glu Val Asp Arg  
 100 105 110

Glu Lys Ser Ala Asn Glu Ser Ala Ser Asn Gly Asn Arg Asn Val Asn  
 115 120 125

Asn Asp Val Asp Glu Thr Ala Arg Val Lys Asp Gln Ser Asn Ala Asp  
 130 135 140

Glu Leu Gly Glu Glu Lys Gly Gln Ala Gln His Gly Glu Gln Val Asn  
 145 150 155 160

Glu Gln Thr Thr Glu Val Ile Ser Leu Leu Ser Asp Asp Glu Glu Asn  
 165 170 175

Gly Ser Asp Ser Leu Val Lys Cys Pro Ile Cys Phe Glu Arg Met Glu  
 180 185 190

Leu Asp Val Leu Gln Gly Lys His Ile Asp Asp Cys Leu Ser Gly Lys  
 195 200 205

Ser Thr Lys Arg Thr Pro Thr Asp Ile Leu Ser Pro Lys Ala Lys Arg  
 210 215 220

Pro Lys Gln Ile Thr Ser Phe Phe Lys Pro Thr Ile Asp Thr Lys Thr  
 225 230 235 240

Pro Ser Pro Pro Thr Ser Lys Ala Ser Thr Thr Pro Thr Ala Thr Pro  
 245 250 255

Thr Thr Thr Leu Leu Lys Ala Asn Val Ala Ser Pro Ser Pro Val Ala  
 260 265 270

Gln Ser Thr Val His Lys Gly Lys Pro Leu Pro Lys Leu Asp Phe Ser  
 275 280 285

Ser Leu Ser Thr Gln Lys Ile Lys Ala Lys Leu Ser Asp Leu Lys Leu  
 290 295 300

Pro Thr Thr Gly Ser Arg Asn Glu Met Glu Ala Arg Tyr Leu His Tyr  
 305 310 315 320

Tyr Val Ile Tyr Asn Ala Asn Leu Asp Ser Asn His Pro Val Lys Glu  
 325 330 335

Ser Ile Leu Arg Gln Gln Leu Lys Gln Trp Glu Met Val Gln His Gln  
 340 345 350

Pro Ser Phe Gly Asp Ala Glu Trp Lys Gly Ala Glu Thr Gly Asn Trp  
 355 360 365

Lys Glu Leu Ile Ala Arg Ala Arg Ser Asn  
 370 375

<210> 89

<211> 764

&lt;212&gt; DNA

<213> *Candida albicans*

&lt;400&gt; 89

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gtaattgtta tattttacca aggtaacagg ggacctcatt atcattagtt gtcaattcaa 60
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atcaggataa aagaattttt ttggttaaag aaaattacag ggacggtaaa tcattcttct 180
tccctataaa ccaaaaatct tatatgtccc aagttaactt attagaattc caagattatt 240
tactttacag tgaatcatta aacattttta ttgaaagcga gtttagctca atgtcttcag 300
acacaactgc ttttcaggca ccaccaacaa aagcaccaga agcctccatg gatctgggta 360
caattcccaa aagatctcca gcaagattgt ttcaaagggtg gatatcatca tcatcatcaa 420
aagataagcc agtatatgca gaaaaagccc ttctcaagaa gcaaaacata gcaccggaac 480
caataaaaaat aactaaacaa caagtaccag ctaaaccaat aggtacatct gaaccatcgt 540
cgcctctaag tgtggcttcg agtcatgata attcatgttc cgattcaagt gcagcttcta 600
tattttctga ttctaaaaat aacaatagta tgcaaatgtt actcacagat gatatagagg 660
acataattaga ggacatagac gatgctgaga tatacgtatg tgagaagggt accataacat 720
atataagttc taaatcatgc taatacacat tattaattat ttga 764

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&lt;210&gt; 90

&lt;211&gt; 179

&lt;212&gt; PRT

<213> *Candida albicans*

&lt;400&gt; 90

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Met Ser Gln Val Asn Leu Leu Glu Phe Gln Asp Tyr Leu Leu Tyr Ser
  1              5              10              15

Glu Ser Leu Asn Ile Leu Ile Glu Ser Glu Phe Ser Ser Met Ser Ser
      20              25              30

Asp Thr Thr Ala Phe Gln Ala Pro Pro Thr Lys Ala Pro Glu Ala Ser
      35              40              45

Met Asp Ser Gly Thr Ile Pro Lys Arg Ser Pro Ala Arg Leu Phe Gln
      50              55              60

Arg Trp Ile Ser Ser Ser Ser Lys Asp Lys Pro Val Tyr Ala Glu
      65              70              75              80

Lys Ala Leu Leu Lys Lys Gln Asn Ile Ala Pro Glu Pro Ile Lys Ile
      85              90              95

Thr Lys Gln Gln Val Pro Ala Lys Gln Ile Gly Thr Ser Glu Pro Ser
      100             105             110

Ser Pro Leu Ser Val Ala Ser Ser His Asp Asn Ser Cys Ser Asp Ser
      115             120             125

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Ser Ala Ala Ser Ile Phe Ser Asp Ser Lys Asn Asn Asn Ser Met Gln  
 130 135 140

Met Leu Leu Thr Asp Asp Ile Glu Asp Ile Leu Glu Asp Ile Asp Asp  
 145 150 155 160

Ala Glu Ile Tyr Asp Ala Glu Lys Val Thr Ile Thr Tyr Ile Ser Ser  
 165 170 175

Lys Ser Cys

<210> 91

<211> 2154

<212> DNA

<213> Candida albicans

<400> 91

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 ttggcagttc ctgtgttag cgttgacaac caagactttg tattgataag agaccttgcc 180  
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 ccattaaccc attcactttt caatagtatc aactcaatgt cgaagctaaa ctattacaag 720  
 aattttggag ttccaggtta ccgatttctt cccaacagca agttatctta tgcagaacga 780  
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 gatccgaact ccatagattt aagcgagtca gtgattccgg gacaagggtt tatacctgac 960  
 tttagtatcc accatctttg caaagtccct aattattatg tgacatcaaa ccaccaaagt 1020  
 ctcccgtgt cgttcaacac aaagaatctt aatgcaactt cgaactcttc gtatttgttt 1080  
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 ttagtccacg aaaagtttga caagaacttt gttgagtact tgctttctga gcaacgcaag 1380  
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 aacccagcac cacctccaca gccaatgag acaccacagt tggatcttaa caacaagttt 1920  
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<210> 92

<211> 717

<212> PRT

<213> Candida albicans

<400> 92

Met Ser Ile Thr Val Thr Phe Pro Lys Ser Pro Ser Thr Lys Lys Arg  
 1 5 10 15

Ala Pro Ala Phe Gly Ile Glu Leu Glu Phe Ser Gln Gln Gly Ser Ser  
 20 25 30

Asp Gly Ala Ile Glu Lys Ala Ala Leu Ala Val Pro Val Phe Ser Val  
 35 40 45

Asp Asn Gln Asp Phe Val Leu Ile Arg Asp Leu Ala Lys Tyr Trp Gly  
 50 55 60

Tyr Pro Ser Ser Tyr Gln Leu Ile Val Lys Leu Val Lys Cys Ala Asn  
 65 70 75 80

Ile Glu Lys Ser Gln Ile Leu Lys Thr Asp Lys Asp Leu Asn Lys Glu  
 85 90 95

Leu Phe Glu Leu Asp Leu Ile Glu Glu Ala Asp Thr Lys Ile Asp Leu  
 100 105 110

Phe Tyr Ile Ser Leu Pro Leu Val Tyr Ser Arg Ile Glu Asn Lys Lys  
 115 120 125

Val Phe Tyr Val Ser Arg Glu Pro Glu Gln Pro Lys Val Ser Lys Ala  
 130 135 140

Pro Thr Gln Glu Lys Pro Ala Ser Val Val Ala Ala Glu Glu Asp Asp  
 145 150 155 160

Asp Asn Leu Asp Asp Asp Glu Glu Asp Glu Val Asp Glu Asp Met Asp  
 165 170 175

Glu Asp Asn Asp Asn Ser Gly Glu Leu Ser Lys Gly Tyr Lys His Met

112

435	440	445
Asn Phe Val Glu Tyr Leu Leu Ser Glu Gln Arg Lys Tyr Thr Glu Asp		
450	455	460
Tyr Ser Asn Leu Glu Ile Leu His Asn Ser Leu Gln Phe Asn Val Leu		
465	470	475 480
Leu Asn Thr Tyr Arg Gly Val Ala Gln Glu Thr Trp Asn Asn Tyr Tyr		
485	490	495
Lys Phe Lys Leu Ile Asp Phe Glu Gln Leu Lys Ala Leu Gln Met Glu		
500	505	510
Ala Asn Glu Leu Glu Glu Arg Lys Leu Asp Ala Ala Arg His Gln Gln		
515	520	525
Trp Ala Glu Glu Glu Lys Leu Arg Gln Glu Arg Leu Arg Leu Val Phe		
530	535	540
Glu Asp Glu Arg Asn Glu Phe Glu Gln Leu Gln Ser Glu Phe Gly Gln		
545	550	555 560
Arg Lys Lys Asp Leu Tyr Glu Lys Leu Arg Arg Arg Gln Leu Glu Ala		
565	570	575
Ser Leu Ser Asp Ser Phe Glu Ala Asp Ser Glu Asn Asp Asp Glu Ser		
580	585	590
Glu Leu Ala Gln Ile Gln Gln Asp Phe Glu Ser Ser Ala Asn Ala Leu		
595	600	605
Lys Thr Lys Phe Glu Ala Lys Arg Lys Asp Leu Ile Asn Pro Ala Pro		
610	615	620
Pro Pro Gln Pro Ile Glu Thr Pro Gln Leu Asp Leu Asn Asn Lys Phe		
625	630	635 640
Ser Leu Pro Thr Val Tyr Pro Glu Ile Ile Arg Asn Leu Pro Leu Glu		
645	650	655
Leu Arg Gly Ile Val Gln Glu Ser Lys Glu Glu Leu Pro Pro Ile Lys		
660	665	670
Lys Pro Ile Leu Tyr Val Thr Thr Tyr Pro Glu Arg Pro Asn Pro Glu		
675	680	685
Tyr Leu Thr Arg Ile Glu Ile Ile Lys Leu Pro Asn Ala Asn Ser Val		



690

695

700

Gly Trp Asp Asn Phe Lys Lys Tyr Lys Asp Ser Asp Val  
 705 710 715

&lt;210&gt; 93

&lt;211&gt; 411

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 93

atgaatagat tcttattcaa ctgtttatta ttcattgggt tacttttaat atacaaatat 60  
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 ggggaattac aagttaaatt aggagataaa ttctttccca tttcaagatt tgctaaacct 180  
 catgctgttg ttcaccctgc tgatcaccat tcgaaagttg atgccaacaa gttccccgat 240  
 gttgaaccag aacaaaaaca aaaagaggat ttaaaagagt ttaaccaaca agtcttaaag 300  
 cctgacatta ataaacaaa ggttgatcct aattcatttc cagatattga accagaggct 360  
 aaagaaagag aagccaaatt aaaagctgaa agacttaaaa agagccaata a 411

&lt;210&gt; 94

&lt;211&gt; 136

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 94

Met Asn Arg Phe Leu Phe Asn Cys Leu Leu Phe Ile Gly Leu Leu Leu  
 1 5 10 15

Ile Tyr Lys Tyr Leu Phe Met Ser Ala Asp Gly Lys Lys Glu Asp Ile  
 20 25 30

Leu Glu Thr Gly Glu Lys Ile Asp Gly Glu Leu Gln Val Lys Leu Gly  
 35 40 45

Asp Lys Phe Phe Pro Ile Ser Arg Phe Ala Lys Pro His Ala Val Val  
 50 55 60

His Pro Ala Asp His His Ser Lys Val Asp Ala Asn Lys Phe Pro Asp  
 65 70 75 80

Val Glu Pro Glu Gln Lys Gln Lys Glu Asp Leu Lys Glu Phe Asn Gln  
 85 90 95

Gln Val Leu Lys Pro Asp Ile Asn Lys Pro Lys Val Asp Pro Asn Ser  
 100 105 110

Phe Pro Asp Ile Glu Pro Glu Ala Lys Glu Arg Glu Ala Lys Leu Lys

115

120

125

Ala Glu Arg Leu Lys Lys Ser Gln

130

135

&lt;210&gt; 95

&lt;211&gt; 1193

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 95

tgacataaaa cgtgtaacca ctacccaaaa gtgtatgttt aaaatactgt ataaacaaaa 60  
 ccaccctatt ctctgaacat tgaatcaact ttaagtttac tgttgataaa ttaagcaaa 120  
 actttgcttc aaattcatat taaaatttta aaaacaattg atccatccat atttctttgc 180  
 tgccagccat cttctttttc tgggttaagtc ttacacgact caagtgtgta aagttttttt 240  
 tttttgctac acgtcttgaa ttttttttcc tttcagaaat tttatatatt gaagccaatt 300  
 tcatttcgaa cttaatcatt tttttttata aatatttagc aaaataatta gccatatcaa 360  
 ttacaaataa tttttacatt tgaataaacc cagataaact ttcaaatacca tcctagcacc 420  
 ttcataatcc attctatata tttgcttctt tattgtctac agtcatttcc gttgcaatgt 480  
 cctcttctaa tgatacacca tctttatttg tcacaccaca aacaccacca agacagcaac 540  
 aaaggagaaa aagtaataca ggagctatat ctacaccctg tgcctcatca gtattattaa 600  
 ctccatctac aacaacaaaa aaacctacaa gaactccagt atcacagaaa agaaaacaag 660  
 gtgtacagtt gtctccacca caggcaaaca aattcccctt tactccaatc acccctcaaa 720  
 aatcaccatg caagacaaga aagaatttgg atttattcac tagtaacgaa aaatttgggt 780  
 tattgttacc atcgccatcc actattgggt ctggtagatg tcataactct ttcacgcaag 840  
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 atgacacaca tatggaattg ataaacagta aaactggtaa gaaaagagtt gtaaagttaa 1140  
 caaagaatca aatgaaaatc aaaccaaaga gattatcggt tgataatata taa 1193

&lt;210&gt; 96

&lt;211&gt; 238

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 96

Met Ser Ser Ser Asn Asp Thr Pro Ser Leu Phe Val Thr Pro Gln Thr  
 1 5 10 15

Pro Pro Arg Gln Gln Gln Arg Arg Lys Ser Asn Thr Gly Ala Ile Ser  
 20 25 30

Thr Pro Val Ala Ser Ser Val Leu Leu Thr Pro Ser Thr Thr Thr Lys  
 35 40 45

Lys Pro Thr Arg Thr Pro Val Ser Gln Lys Arg Lys Gln Gly Val Gln  
 50 55 60  
 Leu Ser Pro Pro Gln Ala Asn Lys Phe Pro Phe Thr Pro Ile Thr Pro  
 65 70 75 80  
 Gln Lys Ser Pro Cys Lys Thr Arg Lys Asn Leu Asp Leu Phe Thr Ser  
 85 90 95  
 Asn Glu Lys Phe Gly Leu Leu Leu Pro Ser Pro Ser Thr Ile Gly Ser  
 100 105 110  
 Gly Arg Cys His Asn Ser Phe Thr Gln Ala Pro Pro Pro Leu Phe Asp  
 115 120 125  
 Leu Lys Lys Val Asn Glu Phe Lys Val Pro Lys Thr Pro Ala Lys Gln  
 130 135 140  
 Ile Ile Asp Asn Ser Arg Thr Lys Glu Ser Glu Asn Glu Asp Asp Trp  
 145 150 155 160  
 Glu Val Met Asp Ile Asp Glu Val Ala Lys Ile Pro Arg Ala Lys Leu  
 165 170 175  
 Arg Asn Pro Phe Ile Asp Thr Phe Glu Pro Thr Ser Pro Val Thr Pro  
 180 185 190  
 Glu Glu Ser Thr Gly Asp Arg Ile Asn Tyr Asp Thr His Met Glu Leu  
 195 200 205  
 Ile Asn Ser Lys Thr Gly Lys Lys Arg Val Val Lys Leu Thr Lys Asn  
 210 215 220  
 Gln Met Lys Ile Lys Pro Lys Arg Leu Ser Phe Asp Asn Ile  
 225 230 235

&lt;210&gt; 97

&lt;211&gt; 888

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 97

atgcaattct caccgctgt cgttttatcc gctgttgctg gttccgcttt ggctgcttac 60  
 tccaactcca ctgttactga cattcaaacc actgttgctc ccatcacttc atgtgaagaa 120  
 aacaaatgtc acgaaactga agttaccact ggtgttacca ccgtcactga agttgacact 180  
 acgtadacca cctactgccc attgtcaacc actgaagctc cagctccatc tactgctact 240  
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gctgtcacca cgggtgtcac cactgtcact gaaggtacta ccatctacac tacctactgc 360  
 ccattgccat ctactgaagc tccagggtcca gctccatcta ctgctgaaga atctaaacca 420  
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 gctgaatctt cccagctca agaaaccact ccaaagaccg ttgctgctga atcttcttca 540  
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 aagggttatt tactattaat tgataaattt atggtttcat gttaatgtac cctttttttt 780  
 ataaacattg ttattattat tatcatcatt agtttattta tattttcgtg aggttttccg 840  
 gtttaattaa attttttgga tacatattaa aaatttattt ggtactag 888

&lt;210&gt; 98

&lt;211&gt; 213

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 98

Met Gln Phe Ser Ser Ala Val Val Leu Ser Ala Val Ala Gly Ser Ala  
 1 5 10 15

Leu Ala Ala Tyr Ser Asn Ser Thr Val Thr Asp Ile Gln Thr Thr Val  
 20 25 30

Val Thr Ile Thr Ser Cys Glu Glu Asn Lys Cys His Glu Thr Glu Val  
 35 40 45

Thr Thr Gly Val Thr Thr Val Thr Glu Val Asp Thr Thr Tyr Thr Thr  
 50 55 60

Tyr Cys Pro Leu Ser Thr Thr Glu Ala Pro Ala Pro Ser Thr Ala Thr  
 65 70 75 80

Asp Val Ser Thr Thr Val Val Thr Ile Thr Ser Cys Glu Glu Asp Lys  
 85 90 95

Cys His Glu Thr Ala Val Thr Thr Gly Val Thr Thr Val Thr Glu Gly  
 100 105 110

Thr Thr Ile Tyr Thr Thr Tyr Cys Pro Leu Pro Ser Thr Glu Ala Pro  
 115 120 125

Gly Pro Ala Pro Ser Thr Ala Glu Glu Ser Lys Pro Ala Glu Ser Ser  
 130 135 140

Pro Val Pro Thr Thr Ala Ala Glu Ser Ser Pro Ala Lys Thr Thr Ala  
 145 150 155 160

Ala Glu Ser Ser Pro Ala Gln Glu Thr Thr Pro Lys Thr Val Ala Ala

	165		170		175
Glu S r Ser Ser Ala Glu Thr Thr Ala Pro Ala Val Ser Thr Ala Glu					
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Ala Gly Ala Ala Ala Asn Ala Val Pro Val Ala Ala Gly Leu Leu Ala					
	195		200		205
Leu Ala Ala Leu Phe					
	210				

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<211> 977
<212> DNA
<213> Candida albicans
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ttacaccacc tataaatata aacaatgtca aaagacgaat atttcggttaa acctagtgggt	180
ccaccacca attataataa tcaaccccaa tcacaacaac cacaacaaag ttatgtacca	240
caatcacaa ccaattattc tcaacaaaca caagatcgag ggatgttttag tgggtgggtgg	300
gggtggcatg gccactatca acaacaacaa ggatataatg cttatggacc accacctcca	360
caagggtgat attatcaaca acagccagggt ggtgggtgggt gatattatca acaacaacaa	420
caacaacaac ctatgtatgt acaacaacaa ccacgttctg gaggtaatga ttcttgttta	480
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ttatttaata ttattgctaa tattactgct attacgacta tatcactttc aagaaatgaa	720
atgaaattta atttaattac aagatttgtt gaaatctttc cttttttttt tttttttttg	780
ctattttaatt aatttacata taaagggttt actcctattc cttttgagta tgttattata	840
attaatgggt attaatatat tcttcaatta agttccacta tgatgttttg gtgggtgggtg	900
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<210> 100
<211> 129
<212> PRT
<213> Candida albicans
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<400> 100
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Tyr Asn Asn Gln Pro Gln Ser Gln Gln Pro Gln Gln Ser Tyr Val Pro
      20             25             30

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Gln Ser Gln Pro Asn Tyr Ser Gln Gln Thr Gln Asp Arg Gly Met Phe  
 35 40 45

Ser Gly Gly Gly Gly Gly His Gly His Tyr Gln Gln Gln Gln Gly Tyr  
 50 55 60

Asn Ala Tyr Gly Pro Pro Pro Gln Gly Gly Tyr Tyr Gln Gln Gln  
 65 70 75 80

Pro Gly Gly Gly Gly Gly Tyr Tyr Gln Gln Gln Gln Gln Gln Pro  
 85 90 95

Met Tyr Val Gln Gln Gln Pro Arg Ser Gly Gly Asn Asp Ser Cys Leu  
 100 105 110

Met Gly Cys Leu Ala Ala Leu Cys Val Cys Cys Thr Leu Asp Met Leu  
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Phe

<210> 101

<211> 2994

<212> DNA

<213> Candida albicans

<400> 101

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&lt;210&gt; 102

&lt;211&gt; 952

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 102

Met Thr Leu Pro Ile Gln Asp Leu Glu Pro Asp Tyr Tyr Ile Ser Val

1 5 10 15

Asn Tyr Pro Thr Thr Asp Asn Gly Ser Pro Thr Pro Gln Ala Glu Lys

20 25 30

Ser Leu Lys Thr Leu Ile Asp Leu Leu Tyr Asp Lys Gly Phe Ala Ala

35 40 45

Gln Ile Arg Pro Gly Asp Leu Asp His Leu Leu Val Phe Val Lys Leu

50 55 60

Ser Ser Tyr Lys Phe Ser Glu Glu Ala Glu Lys Asp Leu Ile Lys Asn  
 65 70 75 80  
 Tyr Glu Phe Gly Val Thr Gly Lys Asp Asp Val Leu Ala Ser Lys Leu  
 85 90 95  
 Arg Ile Ile Tyr Gln Tyr Leu Thr Tyr Pro Gln Ser Val Gly Gly Cys  
 100 105 110  
 Gly Ile Thr Pro Asn Ser Gly Asp Trp Lys Phe Val Thr Ser Ile Val  
 115 120 125  
 Pro Ile Thr Asn Ala Phe Asn Glu Thr Thr Leu Val Glu Asp Leu Lys  
 130 135 140  
 Ile Asn Val Thr Gln Pro Asn Leu Ser Ile Ala Thr Ile Lys Lys Thr  
 145 150 155 160  
 Tyr Gly Val Glu Val Ala Leu Tyr Phe Glu Tyr Ile Lys His Tyr Thr  
 165 170 175  
 Phe Trp Leu Leu Leu Leu Ser Ile Ile Gly Leu Val Ser His Phe Arg  
 180 185 190  
 Lys Asp Lys Arg Phe Ser Leu Thr Phe Ala Phe Ile Asn Leu Leu Trp  
 195 200 205  
 Gly Val Leu Phe Leu Ala Ser Trp His Arg Arg Glu Gln His Leu Val  
 210 215 220  
 Asn Val Trp Gly Val Gln Asn Ser His Leu Ile Glu Glu His Asn Ser  
 225 230 235 240  
 Glu Leu Ala Lys Val Asn Glu Arg Tyr Glu Glu Lys Ser Thr Tyr Phe  
 245 250 255  
 His Ala Asn Asn Thr Asn Gly Phe Arg Phe Leu Lys Gln Leu Ala Phe  
 260 265 270  
 Ile Pro Ile Ala Leu Val Phe Val Gly Val Leu Ile Ser Tyr Gln Leu  
 275 280 285  
 Ser Cys Phe Cys Ile Glu Ile Phe Leu Thr Asp Ile Tyr Asp Gly Pro  
 290 295 300  
 Gly Lys Ser Leu Leu Thr Leu Leu Pro Thr Val Leu Ile Ser Val Phe  
 305 310 315 320



Val Pro Ile Leu Thr Ile Val Tyr Asn Ala Val Thr Asp Ile Ile Ile  
 325 330 335  
 Lys Trp Glu Asn His Asp Asn Gln Tyr Ser Lys Asn Asn Ser Ile Leu  
 340 345 350  
 Val Lys Thr Phe Val Leu Asn Phe Leu Thr Gly Tyr Val Pro Leu Ile  
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 Ile Thr Ser Phe Ile Tyr Leu Pro Phe Ala His Leu Val Gln Pro His  
 370 375 380  
 Leu Gly Asp Ile Lys Thr Thr Ile Ala Thr Tyr Ala Gly Glu Asn Arg  
 385 390 395 400  
 Phe Tyr Thr Lys Tyr Leu Leu Lys Leu Lys Ser Gln Glu Glu Phe Lys  
 405 410 415  
 Ile Asn Gln Gly Arg Leu Asp Ala Gln Phe Phe Tyr Phe Ile Val Thr  
 420 425 430  
 Asn Gln Val Ile Gln Leu Val Leu Lys Tyr Ile Leu Pro Leu Gly Leu  
 435 440 445  
 Arg Phe Val Phe Asn Phe Ile Glu Thr Lys Ile Gln Lys Lys Pro Gln  
 450 455 460  
 Leu Gln Thr Lys Asp Asp Asn Pro Asp Glu Ser Ile Trp Leu His Asn  
 465 470 475 480  
 Val Arg Leu Ser Leu Lys Leu Pro Glu Tyr Asn Val Asp Asp Asp Phe  
 485 490 495  
 Arg Gly Leu Val Leu Gln Phe Gly Tyr Leu Ile Met Phe Gly Pro Val  
 500 505 510  
 Trp Pro Leu Ala Pro Leu Val Cys Ile Ile Phe Asn Leu Ile Phe Phe  
 515 520 525  
 Lys Leu Asp Asn Phe Lys Leu Leu Asn Gly Lys Tyr Phe Lys Pro Pro  
 530 535 540  
 Val Pro Arg Arg Val Asp Ser Ile His Pro Trp Asn Leu Ala Leu Phe  
 545 550 555 560  
 Leu Leu Ala Trp Ile Gly Ser Ile Ile Ser Pro Val Val Thr Ala Phe  
 565 570 575

Tyr Arg His Gly Thr Ala Pro Pro Lys Ser Met Gly Gln Phe Ala Leu  
 580 585 590

Asp Lys Ala Ser Val His Val Ser Ser Ser Val Phe Leu Val Leu Leu  
 595 600 605

Met Phe Val Ser Glu His Gly Phe Leu Ile Leu Ser Tyr Leu Leu Phe  
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Glu Phe Ser Ser Leu Phe Lys Ser Gln Val Glu Trp Glu Asn Asp Phe  
 625 630 635 640

Val Asp Asn Asp Ile Lys Leu Arg His Asp Tyr Tyr Ser Gly Lys Val  
 645 650 655

Lys Pro Thr Tyr Lys Val His Ser Asp Glu Leu Trp Glu Lys Phe Thr  
 660 665 670

Pro Gln Ser Thr Leu Asn Phe Thr Val Pro Lys Pro Thr Ala Glu Thr  
 675 680 685

Asp Asp Lys Val Glu Lys Ile Ala Ser Thr Glu Gly Ala Tyr Ser Thr  
 690 695 700

Ser Ala Glu Lys Ser Thr Thr Thr Ala Thr Ser Arg Ser Asp Lys Ser  
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Lys Ile Leu Ala Glu Lys Glu Ala Ile Leu Lys Gln Lys Glu Ala Glu  
 725 730 735

Leu Ala Glu Leu Glu Lys Lys Lys Thr Lys Leu Asn Asp Phe Lys Asp  
 740 745 750

Pro Thr Asp Ser Val Ile Lys Thr Lys Ser Ser Ala Asn Gly Lys Ala  
 755 760 765

Val Leu Ser Thr Ile Asp Asn Asn Lys His Val Ser Asp Ile Asp Pro  
 770 775 780

Asp Ala Ala Ala Ala Ala Thr Ala Thr Ser Thr Ala Asn Asp Ser Gly  
 785 790 795 800

Ala Lys Lys Ser Thr Ser Thr Ser Thr Ser Ala Ala Thr Asp Thr Thr  
 805 810 815

Asn Thr Ala Pro Ser His Ser Gly Pro Thr Pro Val Thr Ser Ser Glu  
 820 825 830

Lys S r Asn Asn Asn Asn Asn Ser Lys Pro S r Asp Ser Thr Lys Ser  
835 840 845

Thr Leu Ala Asn Asp Glu Thr Arg Lys Thr Leu Asp Pro Lys Gly Val  
850 855 860

Gly Ser Thr Thr Thr Gly Asp Lys Asp Thr Val Ser Ser Asp Lys Ala  
865 870 875 880

Ser Ser Pro Ile Glu Asp Lys Glu Ser Ser Pro Ser Leu Ala Gly Ser  
885 890 895

Ser Thr Ser Thr Pro Ser Gly Thr Asp Lys Lys Thr Ser Pro Lys Lys  
900 905 910

Leu Val Thr Asn Ala Val Asn Lys Val Glu Asn Asn Asp Asp Phe Lys  
915 920 925

Lys Phe Ile Asn Glu Ala Glu Lys Glu Ala Lys Lys Ser Lys Ser Gly  
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Leu Lys Lys Leu Phe Asn Lys Lys  
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<210> 103

<211> 72

<212> PRT

<213> Candida albicans

<400> 103

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Leu Ser Leu Met Ile Ser Val Gln Lys Asn Gln His Gln His Gln His  
20 25 30

Gln Gln Pro Gln Ile Leu Leu Thr Ser Pro His Leu Ile Ser Val Gln  
35 40 45

Leu Ser Ser Leu Leu Ser Lys Asn Gln Thr Thr Thr Thr Val Ser  
50 55 60

Gln Val Ile Val Pro Asn Leu Leu  
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&lt;210&gt; 104

&lt;211&gt; 4809

&lt;212&gt; DNA

<213> *Candida albicans*

&lt;400&gt; 104

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 gtccgtgtg

4809

&lt;210&gt; 105

&lt;211&gt; 1603

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 105

Met Val Cys Lys Glu Gly Leu Pro Ser His Lys Leu Tyr Asp Glu Lys

. 1

5

10

15

Leu Gly Lys Glu Ile Asp Leu Lys Asp Phe Arg Arg Gly Ile S r Phe  
 20 25 30  
 Lys Val Phe Asp Phe Ser Val Thr Tyr Lys Leu Ala Arg Lys His Phe  
 35 40 45  
 Glu Thr Ser Val Ala Leu Leu Lys Ala Phe Thr Leu Ser Glu Tyr Ala  
 50 55 60  
 Ser Glu Tyr Ile Glu Asp Phe Asp Lys Val Thr Glu Val Gln Val Ser  
 65 70 75 80  
 Glu Ser Glu Ile Ser Asp Leu Ser Ser Ile Asn Ser Ala Glu Ser Ile  
 85 90 95  
 Pro Leu Asn Asp Ala Ser Pro Ser Glu Leu Asp Glu Ser Asn Thr Lys  
 100 105 110  
 Lys Ile Lys Thr Val Leu Thr Val Arg Asp Ile Leu Val Ser Asn Ala  
 115 120 125  
 Gly Lys Ser Asp Glu Lys Asp Pro Asp Arg Leu Thr Leu Ser Ile Pro  
 130 135 140  
 Glu Val Asp Gly Arg Val Asp Met Phe Leu Val Trp Cys Cys Phe Tyr  
 145 150 155 160  
 Ala Lys Thr Met Leu Glu Arg Phe Lys Pro Thr Val Glu Ser Ser Cys  
 165 170 175  
 Thr Lys Asn Gln Ile Lys Ile Ile Arg Gly Pro Arg Lys Lys Leu Lys  
 180 185 190  
 Leu Asp Val His Leu Asp Ser Val Ala Leu Val Ile Arg Leu Pro Arg  
 195 200 205  
 Lys Val Asp Val Met Ile Glu Ile Asp Arg Ala Arg Leu Lys Asn Ala  
 210 215 220  
 Leu Val Leu Lys Ser Ala Asp Ile Val Asn Cys Arg Leu Tyr Val Val  
 225 230 235 240  
 Asp Pro Ser Thr Lys Phe Trp Ala Arg Leu Leu Ile Ile Lys Glu Pro  
 245 250 255  
 Lys Phe Ser Ile Asp Phe Thr Lys Ser Ile His Asp Ala Tyr Phe Gly  
 260 265 270

Ile Ser Thr Arg Ser Ile Arg Ile Ser Val Pro Asn Arg Phe Leu Phe  
 275 280 285  
 Tyr Thr Val Ile Asp Asn Phe Ile Thr Phe Phe Lys Ala Ile Lys Gln  
 290 295 300  
 Leu Ser Gln Asn Phe Arg Tyr Phe Asn Trp Gly Ile Asp Glu Phe Glu  
 305 310 315 320  
 Thr Ile Tyr Pro Ser Gln Lys Asn Ala Ile Val Phe Pro His Val Asn  
 325 330 335  
 Ile Lys Thr Ala Val Leu Gly Met Glu Leu Arg Ala Asp Pro Phe Glu  
 340 345 350  
 Asn Lys Leu Ala Leu Ile Phe Glu Leu Gly Lys Ile Glu Gln Lys Glu  
 355 360 365  
 Arg Ile Arg Lys Trp Lys Ala Phe Glu Lys Lys Ser Gln Glu Ile Leu  
 370 375 380  
 Asp Gly Val Glu Ser Asn Ile Glu Asp Gln Ile Glu Leu Ser Asn Ile  
 385 390 395 400  
 Ala Ala Pro Ile Pro Ser Pro Ala Pro Ile Ala Ser Lys Thr Thr Thr  
 405 410 415  
 Ser Thr Met Thr Pro Asn Val Ala Gly Asp Ser Ile Thr Arg Pro Asp  
 420 425 430  
 Ser Pro Pro Arg Ser Gly Ser Ser Glu Cys Ser Phe Thr Ser Gly Ala  
 435 440 445  
 Gly Leu Ile Lys Asn Lys Leu Leu Asn Arg Lys Lys Pro Thr Lys Thr  
 450 455 460  
 Ser Val Asn Gly Val Ala Pro Val Asn Glu Ile Glu Pro Ala Asp Ala  
 465 470 475 480  
 Lys Tyr Thr Val Glu Glu Ala Glu Glu Arg Ile Ala Glu Ala Lys Glu  
 485 490 495  
 Arg Leu Phe Glu Asn Phe Ser Lys Ser Trp Cys Arg Lys Tyr Arg Val  
 500 505 510  
 Phe Glu Glu Thr Lys Cys Arg Lys Trp Lys Glu Arg Gly Glu Asn Ile  
 515 520 525

Trp Gly Ser His Asp Ile Asn Glu Val Met Lys Glu Lys Tyr Asp Ile  
530 535 540

Val Glu Tyr Asp His Gly Lys Pro Leu Thr Gly Ala Ile Phe Arg Asp  
545- 550 555 560



Leu Lys Met Asn Gln Ala Glu Val Asn Ile Glu Asn Ala Asp Ala Arg  
 1045 1050 1055  
 Val Ile Tyr Ala Leu Phe Asn Asp Thr Ser Val Thr Gly Lys Leu Met  
 1060 1065 1070  
 Thr Tyr Leu Asn Ala Asp Ser Ser Asp Ser Ser Thr Asp Gly Ser Gln  
 1075 1080 1085  
 Ser Ser Asp Tyr Arg Gly Ser Ser Tyr Ser Arg Trp Leu Glu Asn Val  
 1090 1095 1100  
 Glu Ile Ser Asp Gly Asp Phe Ser Trp Tyr Asp Pro Lys Asp Phe Ile  
 1105 1110 1115 1120  
 Glu Leu Glu Val Arg Glu Pro Leu Ser Pro Tyr Pro Lys Thr Lys Ile  
 1125 1130 1135  
 Leu Pro Phe Phe Ala Thr Pro Lys Phe Ser Tyr Tyr Arg Glu Phe Thr  
 1140 1145 1150  
 Leu Gln Lys Asp Gly Pro Phe Pro Phe Gly Ser Glu Lys Ile His Asp  
 1155 1160 1165  
 Cys Ile Met Asn Leu Asp Lys Pro Ala Ile Val Gln Ser Arg Ile Leu  
 1170 1175 1180  
 Leu Asp Arg Leu Gln Asn Leu Glu Asp Glu Leu Ala His Asn Glu Glu  
 1185 1190 1195 1200  
 Met Leu Arg Arg Phe Lys Ile Gln Asn Gly Pro Glu Phe Gln His Asp  
 1205 1210 1215  
 Ile Arg Met Thr Glu Gln Glu Ile Ser Thr Leu Lys Glu Lys Val Glu  
 1220 1225 1230  
 Val Val Arg Ala Ala Tyr Asn Gly Phe Ser Asp Asp Glu Phe Gly Gly  
 1235 1240 1245  
 Leu Pro Ser Ser Ser Ala Asn Asn Val Ala Asp Asp Asp Asp Gly Ser  
 1250 1255 1260  
 Ser Ser Leu Ser Arg Ser Ser Thr Gly Leu Ser Ala Tyr Ser Ser His  
 1265 1270 1275 1280  
 Val Thr Gln Asp Gln Met Ser Gln Ala Ala Ala Phe Val Ser Ile Ala  
 1285 1290 1295

&lt;210&gt; 113

&lt;211&gt; 2021

&lt;212&gt; DNA

&lt;213&gt; Candida albicans

&lt;400&gt; 113

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gacgtcactg aaacagggga cggatcatta gaggattttg ttgaacattt tactgatgga 180
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gatgatttag acgtgaatga attccttgaat agagttgggtg ctgctgctgg tgcaagatat 420
tccactcaaa cttccggact caaaaaacca tcccctgctg cacctaaacc tacttcaaaa 480
cctgttggtg ctaaattctag ttctgcttca aaaccttcat ttgtaccaa atctactggg 540
aagcctggtg ctccagctaa gccaaaacca aagaacatca ccaaggatgc tggttggggg 600
gatgctgaag acgttgagga aagagacttt gacaagaaac ctttggataa cgttccatcg 660
gcatataaac caacaaaggt taacattgac gaattgagaa aacaaaaatc agatacaact 720
agctcaactc ctaaaacatt caaatctgaa ccacaagaag aaaagaatga cgatgatggg 780
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2021

&lt;210&gt; 114

&lt;211&gt; 648

&lt;212&gt; PRT

&lt;213&gt; Candida albicans

&lt;400&gt; 114

Met Glu Lys Ile Asp Il Asn Thr Asn Ser Asn Lys Ile Gln Gln Ala

138

260 265 270  
 Asp Gln Pro Ser Ser Ser Asp Gly Arg Leu Thr Ser Leu Pro Lys Pro  
 275 280 285  
 Lys Ile Gly His Ser Val Ala Asp Lys Tyr Lys Ala Ser Ala Ser Gly  
 290 295 300  
 Asn Gly Ala Ala Pro Ala Phe Gly Ala Lys Pro Ala Phe Gly Thr Gln  
 305 310 315 320  
 Ser Val Asp Ser Arg Lys Asp Lys Leu Val Gly Gly Leu Ser Arg Asp  
 325 330 335  
 Phe Gly Ala Glu Asn Gly Lys Thr Pro Ala Gln Ile Trp Ala Glu Lys  
 340 345 350  
 Arg Gly Lys Tyr Lys Thr Val Ala Ser Asp Glu Lys Glu Thr Asn Ser  
 355 360 365  
 Ser Glu Lys Val Asp Glu Pro Glu Glu His His Ala Ala Asp Leu Ala  
 370 375 380  
 Lys Lys Phe Glu Glu Lys Ala Asn Ile Ala Gly Asp Thr Pro Ser Leu  
 385 390 395 400  
 Pro Thr Arg Asn Leu Pro Pro Ala Pro Pro Ala Arg Glu Thr Ala Ile  
 405 410 415  
 Pro Ser Asn Glu Lys Asp Lys Xaa Glu Lys Glu Glu Glu Glu Gln Ala  
 420 425 430  
 Pro Ala Pro Ser Leu Pro Thr Arg Asn Leu Pro Pro Pro Ser Gln Arg  
 435 440 445  
 Gln Pro Glu Pro Glu Pro Glu Pro Glu Glu Glu Glu Glu Glu Glu  
 450 455 460  
 Xaa Glu Ala Pro Ala Pro Ser Leu Pro Ala Arg Asn Leu Pro Pro Ala  
 465 470 475 480  
 Pro Lys Ala Glu Ala Glu Glu Ser Lys Lys Gln Ser Thr Thr Ala Thr  
 485 490 495  
 Ala Glu Tyr Asp Tyr Glu Lys Asp Glu Asp Asn Glu Ile Gly Phe Ser  
 500 505 510  
 Glu Gly Asp Leu Ile Ile Asp Ile Glu Phe Val Asp Asp Asp Trp Trp

515 520 525  
Gln Gly Lys His Ala Lys Thr Gly Glu Val Gly Leu Phe Pro Ala Thr  
530 535 540  
Tyr Val Ser Leu Asn Glu Lys Ala Ala Asp Lys Glu Glu Glu Ala Pro  
545 550 555 560  
Ala Pro Ala Pro Ala Pro Ser Leu Pro Ser Arg Glu Glu Thr Gln Ala  
565 570 575  
Ala Pro Ala Leu Pro Ser Arg Ser Glu Gln Lys Pro Glu Ser Lys Thr  
580 585 590  
Ala Thr Ala Glu Tyr Asp Tyr Glu Lys Asp Glu Asp Asn Glu Ile Gly  
595 600 605  
Phe Ser Glu Gly Asp Leu Ile Val Glu Ile Glu Phe Val Asp Asp Asp  
610 615 620  
Trp Trp Gln Gly Lys His Ser Lys Thr Gly Glu Val Gly Leu Phe Pro  
625 630 635 640  
Ala Asn Tyr Val Val Leu Asn Glu  
645